UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY
CIVIL ACTION NO. 06-2003 (FLW)

ROCHE PALO ALTO, LLC, Plaintiff, V. RANBAXY LABORATORIES LIMITED, and RANBAXY, INC., Defendants.	:	TRIAL TRANSCRIPT VOLUME 10 DECEMBER 22, 2008

CLARKSON S. FISHER UNITED STATES COURTHOUSE
402 EAST STATE STREET, TRENTON, NJ 08608

B E F O R E : THE HONORABLE FREDA L. WOLFSON, USDJ

A P P E A R A N C E S :

GIBBONS, P.C.
BY: DAVID E. DeLORENZI, ESQUIRE
SHEILA F. McSHANE, ESQUIRE
-and-
CADWALADER, WICKERSHAM & TAFT, LLP (N.Y.)
BY: GREGORY A. MARKEL, ESQUIRE
TONY PEZZANO, ESQUIRE
BARTHOLOMEW VERDIRAME, ESQUIRE
JEFFREY Z.Y. LIAO, ESQUIRE
MICHAEL P. DOUGHERTY, ESQUIRE
VINNY LEE, ESQUIRE
On behalf of the Plaintiff

MATHEWS, SHEPHERD, McKAY & BRUNEAU, ESQUIRES
BY: ROBERT G. SHEPHERD, ESQUIRE
-and-
KNOBBE, MARTENS, OLSON & BEAR, LLP (CA)
BY: JOSEPH M. REISMAN, ESQUIRE
WILLIAM R. ZIMMERMAN, ESQUIRE
ERIK T. ANDERSON, ESQUIRE
DARRELL OLSON, ESQUIRE
THOMAS P. KRZEMINSKI, ESQUIRE
JOSEPH F. JENNINGS, ESQUIRE
DARRELL L. OLSON, ESQUIRE
CHRISTY G. LEA, ESQUIRE
On behalf of the Defendants

* * * * *

VINCENT RUSSONIELLO, CCR-R
OFFICIAL U.S. COURT REPORTER
138 PAXSON AVENUE, TRENTON, NEW JERSEY 08690
(609) 588-9516

C E R T I F I C A T I O N

PURSUANT TO SECTION 753, TITLE 28 U.S.C., THE FOLLOWING TRANSCRIPT IS CERTIFIED TO BE AN ACCURATE TRANSCRIPTION OF MY STENOGRAPHIC NOTES IN THE ABOVE-ENTITLED MATTER.

S/Vincent Russoniello
VINCENT RUSSONIELLO, CCR-R
OFFICIAL U.S. COURT REPORTER

M O R N I N G S E S S I O N

(In open court.)

THE CLERK: All rise.

THE COURT: Thank you. Everyone may be seated. Good morning.

MR. PEZZANO: Your Honor, we reached, with opposing counsel, a proposal on post-trial briefing. We can talk about that at the end of the day. It's your preference.

THE COURT: Yes. That's fine.

MR. PEZZANO: We understand there is one objection to an exhibit on the first witness, and it's going to be raised before that witness testifies.

As to the final two witnesses, Dr. Maag and Dr. Henck, my understanding is any objections to exhibits may be raised during the course of their examination.

MR. JENNINGS: The objection, your Honor, is to Dr. Stella's testimony about Defendant's Exhibit 459. It's outside of the scope of the expert report. It was not discussed or referenced in Dr. Stella's expert report.

I understand plaintiff's logic. They referred me to a portion of Dr. Stella's report where he

basically says the defendants have offered expert testimony regarding the obviousness of the invention. I disagree. I understand their position that, because he generically disagreed, he can then discuss and testify about anything that might have been referenced in our reports. He did discuss many things that were referenced in our reports -- not this exhibit, not our expert's testimony about this exhibit and report.

THE COURT: What is Defendant's 459?

MR. JENNINGS: Defendant's 459 is a Syntex in-house memorandum about valganciclovir and what they may have done in coming up with that.

MR. VERDIRAME: Your Honor, Exhibit 459 is already in evidence. It was mentioned in Dr. Gokel's expert report and included as an exhibit. Dr. Stella in his expert report says he reviewed the materials identified by Dr. Gokel and the exhibits to Dr. Gokel's expert report and said he disagreed with Dr. Gokel's opinion. That's the reason why it is within the scope of his opinion.

THE COURT: So he made a general reference without specificity.

MR. VERDIRAME: As to that document, yes, your Honor.

MR. JENNINGS: I would doubt there is a

general reference to the document. This is the paragraph they pointed me to:

"Paragraph 106 of Dr. Ranbaxy has presented expert reports that conclude or suggest that the invention of the '953 patent was obvious over the prior art. I disagree."

MR. VERDIRAME: And he says he reviewed the exhibits attached to Dr. Gokel's --

THE COURT: Where does he say that?

MR. VERDIRAME: He doesn't say anything specific. At the end of the report he lists the materials that he reviewed.

THE COURT: Did you depose him?

MR. JENNINGS: Yes, we did. This topic never came up in his deposition.

THE COURT: You didn't ask him about that part of his opinion where he said he disagreed and what he was referring to and what he based that on.

MR. JENNINGS: There is much in his report --

THE COURT: No, in his deposition.

MR. JENNINGS: Not about the generic topic. What plaintiff is referring to there is a list of materials considered in the end, and the materials considered list the expert report of George Gokel.

MR. VERDIRAME: And exhibits.

MR. JENNINGS: With exhibits.

THE COURT: I'm going to let him discuss it. The fact he made this general statement, but it was not gone into and explored, I'll let him talk about it today.

MR. VERDIRAME: Roche calls Dr. Valentino Stella.

THE COURT: You are going to have to set a foundation when he rendered the report and referred to the exhibits, what he was relying on.

MR. VERDIRAME: Okay.

THE COURT: And I want to know when he actually looked at this document in forming his opinions. If it was not until now, during trial, I may change my ruling.

MR. VERDIRAME: Okay, your Honor.

VALENTINO J. STELLA, called as a witness on behalf of the plaintiff, having been first duly sworn, testified as follows:

THE COURT: You may proceed.

MR. VERDIRAME: Your Honor, Dr. Stella is a professor in pharmaceutical chemistry at the

University of Kansas and an expert in the area of prodrugs. He has authored numerous publications with respect to prodrugs. He will explain the difficulties involved in making prodrugs. He will explain that the invention of the '953 patent provides unexpected results with respect to improved oral bioavailability.

DIRECT EXAMINATION

BY MR. VERDIRAME:

Q. Dr. Stella, would you please state your full name and address for the record.

A. Valentino J. Stella, 1135 West Campus Road, Lawrence, Kansas.

Q. Are you currently employed?

A. Yes, I am.

Q. Where are you currently employed?

A. I'm a university Distinguished Professor of pharmaceutical chemistry at the University of Kansas.

Q. Approximately how long have you been at the University of Kansas?

A. I'm in my 36th year at the University of Kansas.

Q. In the binder in front of you is Exhibit PTX-655. Is that your CV?

A. Yes, it is.

Q. Please describe your undergraduate and post-

graduate education for us, Dr. Stella.

A. Yes.

I received a Bachelor of pharmacy degree from the Victorian College of Pharmacology in Melbourne, Australia. I completed the degree in 1967, and the degree was actually conferred in 1968.

After getting my Bachelor's degree and working for one year as a hospital pharmacist, I entered graduate school in the United States. In 1968, I came to the University of Kansas to work on my Ph.D., and I received my Ph.D. from the University of Kansas in 1971.

Q. Did you have a specialty or focus in earning your Ph.D.?

A. My Ph.D. is in analytical pharmaceutical chemistry and pharmaceutics. The work that I did in my Ph.D. work was to the design and evaluation of a prodrug of the anti-seizure drug Dilantin.

Q. Are you the named inventor on any patents?

A. I believe I have approximately 30 patents or applied patents that are being evaluated right now.

Q. Generally, what do your patents relate to?

A. The majority of the patents are on prodrugs. I also had patents on some novel solubilizers, and a couple of patents on controlled drug delivery.

Q. Have any of your patents led to products that have been used by patients?

A. Yes, I have three drug products that are approved by the FDA. The first one is a drug called fosphenytoin. That is a water soluble prodrug of the drug Dilantin, and it is used to treat grand mal seizures.

I also have a drug called viread. I did that in my consulting capacity with a company called Gilead. Viread is an anti-viral drug, and I designed the prodrug portion of that particular drug that made it orally bioavailable.

Fortunately, last Monday I had my third drug approved, and that is a drug called Lusedra, which is a novel anesthetic drug. It's number 3. I was pretty proud of that.

I'm also the inventor of a material called captisol. Captisol is a novel solubilizer. It is currently used in four drug products. Those four drug products are life-saving drugs. One is an anti-fungal drug and two are anti-schizophrenic drug. The fourth drug is a veterinary product. I have two drugs that are in clinical trials. One is called R-788, which is a novel prodrug of a drug called R-406. That's in Phase II-Phase III clinical trials with a company

called Rigel.

And then I have a product called Nanotax, which is a drug to treat metastasize ovarian cancer in women.

Q. Are the publications and textbooks you have authored and the fellowships and honors you have received identified in your CV?

A. They are.

Q. Are any of your books particularly well known in the scientific communities?

A. I would say I have two books in the area of drug stability, and I have two books in the area of prodrugs. Both sets of books have been very well received.

My last book, which was published last year, called "Prodrugs Challenges and Rewards" or "Rewards and Challenges," I forget, actually sold out in its first printing, and it is now in its second printing. It's done very well.

Q. Dr. Stella, are you an expert in the area of drug delivery and prodrugs?

A. Yes, I am.

MR. VERDIRAME: Your Honor, we offer Dr. Stella as an expert in the area of drug delivery and prodrugs.

MR. JENNINGS: No objection, your Honor.

THE COURT: Fine. He will be accepted as an expert in those areas.

MR. VERDIRAME: Thank you.

BY MR. VERDIRAME:

Q. Dr. Stella, what is your understanding of your role in this case?

A. My understanding is that I'm offering an expert opinion on the validity of the '953 patent in light of the prior art and from the point of view of one skilled in the art.

I've also been asked to evaluate the expert reports of Drs. Gokel and Sloan as to the validity or correctness of their assessment of the validity of the '953 patent.

Q. Have you been qualified to testify as an expert by a court before today?

A. Yes, I have.

Q. Are you being compensated for your work today?

A. Yes, I am.

Q. Does your compensation depend on the outcome of this case?

A. No.

Q. Please put PTX-1 on the screen, which is also in the binder in front of you, Dr. Stella.

Do you recognize this exhibit?

A. Yes. This is the patent in suit.

Q. Have you read the expert reports and listened to the opinions of Ranbaxy's experts, Dr. Sloan and Gokel regarding the validity of the '953 patent and whether the invention of the '953 patent produced unexpected results over the prior art?

A. Yes, I have.

Q. Do you agree with Dr. Sloan and Dr. Gokel?

A. No, I do not.

Q. Would you please briefly tell us why not.

A. Well, I think, first, is that both Gokel and Sloan assume that valganciclovir was mentioned in the prior art that was present in the prior art.

Second is that I disagree with Sloan and Gokel that the bioavailability, the superb bioavailability seen with ganciclovir was predicted. It wasn't.

Third is that Gokel and Sloan do not address the issue of the diastereomers and the ability of the diastereomers to in fact form a crystalline material and to show superb bioavailability.

In my opinion, both Sloan and Gokel trivialize the drug discovery and prodrug discovery process. I think their analysis is basically a hindsight analysis.

Q. What does this patent relate to generally, Dr. Stella?

A. This patent relates to the discovery of a novel prodrug of ganciclovir with excellent oral bioavailability and the ability to treat and, therefore, treat in a very good manner anti-viral diseases, especially CMV.

Q. What is "oral bioavailability"?

A. Your Honor, this is relatively technical term, so bear with me. If my discussion is not adequate, please ask questions.

When we give a drug intravenously -- and the abbreviation that we have used is IV. When we give that drug into a vein, we can assume that we are delivering 100 percent of the drug. Why? Because all of the drug is being put directly into the vein.

When we take a drug orally, the drug has to undergo a number of steps, which we will discuss subsequently. And so the amount of drug that can reach what we call the systemic circulation or plasma is limited by a number of barriers.

So when we talk about bioavailability, we are comparing the ability to absorb a drug, let's say, for example, orally and relative to the delivery of that drug given intravenously.

So "oral bioavailability" refers to the fraction of drug that we give that reaches essentially the systemic circulation or the plasma. That experiment, the ability to do that, involves a number of techniques that we do in the laboratory in animals and subsequently also in man.

Q. Can you briefly tell us how oral bioavailability is measured?

A. I have sort of already mentioned that a little bit.

Again, your Honor, essentially what happens if you give a drug intravenously, we can assume 100 percent is delivered; we measure the plasma level, for example, as a function of time and we compare that plasma level time curve to giving the drug orally. We also measure plasma levels, and we compare what's called area under the curve. The abbreviation is AUC.

So we compare the plasma levels that you get from oral delivery to a control, and that control is the intravenous dose. And by comparing the area under the curve from the oral dose to the IV dose, we can then determine what the absolute bioavailability of the drug is. That's essentially how that experiment is performed.

If we do the experiment in experimental

animals, like the rat, for example, you usually can't give the oral dose and the intravenous dose to the same rat. You can, but it's a difficult experiment to do. In humans and in higher animals, we do what's called a cross-over study.

For example, your Honor, if I was to do the bioavailability of ganciclovir in you, the first week I might give you an intravenous dose of ganciclovir, and the second week I would give you the oral dose of ganciclovir, and I would compare the blood levels that we got. For another gentleman like Bart, Mr. Verdirame, I would give him, perhaps, the oral dose first and then the intravenous dose. The advantage of doing that is we have what's called an inpatient control, that is, I can compare how the drug performed in you and how it performed in Mr. Verdirame. It is not easy to do in a rodent animal model. And the importance of that will become obvious a little bit later on.

Q. Dr. Stella, do you have a demonstrative showing the issues involved in trying to develop prodrugs having improved oral bioavailability?

A. Yes, I do.

Q. Please put PTX-683 on the screen.

Is this the demonstrative you are referring

to?

A. Yes, it is.

Q. Please explain for us what PTX-683 shows.

A. What I'm showing here, your Honor, is a drug that has some barrier to its delivery. I'm showing the drug bouncing off the barrier.

I would like to talk a little bit why -- I'm going to focus on why a drug might show very poor oral bioavailability. There are basically four reasons why a drug will show poor oral bioavailability:

One is the drug may not dissolve. That is it never even reaches close to getting into the body. It is not unlike swallowing a piece of sand. The sand is not going to dissolve. The molecule in that case will simply end up in the feces.

The second, let's assume our drug can dissolve. Before it reaches the intestinal barrier, there are enzymes that are designed to basically destroy what we eat in our food.

So, for example, when you possibly had breakfast this morning, you ate certain food products. Right now digestion is going on in your GI tract breaking down those food products; the same way your drug can be destroyed in the contents of the small intestine.

Let's assume our drug does dissolve and does survive. The next barrier would be the ability to cross the cells that line the small intestine. Those cells are called enterocytes. Those enterocytes are there to prevent the absorption of materials the body does not want to absorb.

The fourth barrier is that present in the enterocytes and in the liver are enzymes that are designed to destroy materials that the body does not want to be exposed to. When you had the piece of lettuce maybe in your salad last night, there were materials in that lettuce in your food that the body may decide evolutionarily that is not good for you to get exposed to. So we have developed these enzymes designed to destroy what is called exogeneous materials. So the ability of a drug to get into the body is limited by those four barriers.

And what we do in prodrug research is we say: Well, if this drug has some barrier to its delivery, can we change the properties of this drug by making a prodrug?

That's what's illustrated here on this slide here, your Honor.

Q. Are there difficulties involved in finding a prodrug that will work?

A. Absolutely, and those barriers are legend.

For example, let's assume that the barrier for our delivery here is the inability to cross a membrane. Let's say we identify that.

No. 1 is that very often, early in the development of a drug, we may not know why a drug is performing poorly. So the design of a prodrug is a guessing game or at least an educated guess. So what we do in the case of a prodrug is that we add a promoiety, and the idea here is we change the properties of the drug so that it's able to overcome the particular barrier for the delivery of that drug.

However, in changing the properties of the drug, we are attempting to identify what the barrier is and how that promoiety might help in overcoming that barrier. Assuming that we can deliver the drug into the body through the prodrug, we also then have to clip off the appendage to release the drug. And so designing a prodrug that overcomes all those steps and yet still adequately delivers the drug is quite a heroic task.

Q. Dr. Stella, I would like to ask you about a document which was discussed just prior to your getting on the stand this morning, Exhibit 459. That's in the binder in front of you. It's DX-459.

A. Yes.
Q. Is that a document you reviewed in formulating your opinion?
A. I saw this document prior to the trial. But I really only reviewed it in detail since I have been at the trial.
THE COURT: When you gave your opinions both in your deposition and rendered a report, did you rely on this document in any way?
THE WITNESS: No, I did not.
MR. VERDIRAME: I will not ask further questions about the document.
THE COURT: Very well.
BY MR. VERDIRAME:
Q. Dr. Stella, have you reviewed the claims of the '953 patent in suit?
A. Yes, I have.
Q. Do you have an understanding about what those claims are directed to?
A. They are directed towards valganciclovir hydrochloride in crystalline form. It is a drug that shows excellent bioavailability, and it is useful in the treatment of a number of anti-viral diseases, but namely CMV.
Q. Would one of skill in the art have expected that

valganciclovir hydrochloride in crystalline form would have provided improved oral bioavailability over ganciclovir?

A. No.

Q. Why not?

Perhaps I can ask one further question.

Do you have a demonstrative that would help explain your answer?

A. Yes.

MR. VERDIRAME: Please put the demonstrative 754 on the screen.

MR. WITNESS: Yes. This demonstrative, your Honor, is fairly complicated. So I will try to go slowly and walk you through it.

THE COURT: I'm glad you realized that.

THE WITNESS: If you remember last week, your Honor, we talked about the fact that valganciclovir, which is shown here, two diastereomers, I put a slightly less complicated version of that here, so you can appreciate it. What I'm going to do now is walk you through the process whereby a design prodrug will lead to adequate delivery of the drug.

So let's assume we have -- let's assume the area above this little cartoon is the contents of the small intestine. If I put the two diastereomers in

the content of the small intestine -- I have mentioned earlier today that there are enzymes present in the small intestine that can chew up food products and can adequately chew up drug products. If it does that, then we produce ganciclovir. And ganciclovir we already know is incapable of crossing the biological membrane. So if I get conversion of one or both of the diastereomers in the contents of the small intestine and I produce ganciclovir, I cannot deliver, I cannot improve on the delivery of ganciclovir.

So the first step is: Can I design a prodrug that survives this milieu? Remember, that milieu is designed to destroy exogeneous materials. So let's assume the molecule does survive that. There is no apriority; you cannot predict whether this is going to survive. You can predict whether one of them or both of them are going to survive.

The next step is: Can one or both of these diastereomers cross the biological membrane? These are relatively polar materials; and, so, in all likelihood, if these are going to be absorbed at all, they may have to interact with the stereospecific transport illustrated here.

This is a protein molecule that embedded in the surface of the membrane. Effectively, what these

materials have to do is interact with a very complex molecule and be transported across this membrane.

I have another demonstrative that sort of speaks to the critical nature of this process.

MR. VERDIRAME: Please put Exhibit 755 on the screen for a moment.

THE WITNESS: Your Honor, when Dr. Sloan talked about this process the other day, he stole my thunder because he saw my demonstrative.

Dr. Sloan suggested that an interaction of a drug molecule -- and over here on the right, I'm showing you valacyclovir, which the Ranbaxy experts have assumed incorrectly predicts the behavior of ganciclovir.

So one can think of this molecule interacting with the stereospecific transporter as something like a lock and key. No. 1 is no one knew what the shape of the lock was because if you remember in the Beauchamp papers, they only talked in generalarities about being a stereospecific transporter. Dr. Sloan mentioned what was important was the valine component. I have drawn that here as one of the teeth in the key. Dr. Sloan mentioned this is all that was necessary.

Your Honor, if you have a key and it doesn't have a handle, you can't open the lock. So it is not

the valine that is important; it is the total molecule. This molecule in total has to interact with the stereospecific transporter of unknown origin, of unknown source, and of unknown structure.

So let's consider now that we have valganciclovir -- could I have the next one.

So, effectively, what I have shown you here with this model key is that this component down here is the hydroxymethyl group you heard discussed extensively by both sides.

Now, will this key fit this lock and will it open the lock? It might; it might not. We can't predict from one molecule valacyclovir -- that a structurally structural compound like valganciclovir will interact with the stereospecific transporter. This additional appendage may have a tremendous effect; it may have no effect. We don't know. It's highly unpredictable. The key may fit the lock, but whether it will open the door, I don't know.

I'm not sure what kind of car you drive, your Honor, but you can take your key for your car and maybe someone has a very similar model car; and if you compare the keys, often they look very similar. There is only a little bit of difference in the key. Does your key open the other person's car? It might.

Probably won't. That's by design.

So now we have a problem: Can this compound -- and this is one of the diastereomers.

Can I have the next slide.

If I take the other diastereomer, since we don't know what the shape of the keyhole is, I don't know the shape of the keyhole, so I drew that as a gray area up here. You don't know if this is going to fit. And if it does fit, will it open? And so to assume that valacyclovir predicts -- valganciclovir is a stretch of the imagination. I think it is very much hindsight analysis, and whether the two diastereomers would also interact, one and not both, we wouldn't know that. We wouldn't know that at this time.

I would like to go back to the previous demonstrative, please.

So let's assume in the best case scenario that both of these molecules, one or both, are able to get inside the cell. Now, -- let's assume we are able to get this molecule -- and I don't know whether one or both will. The environment in this cell is called inside the enterocyte, is really designed to break up food products, and exogenous materials. So if I produce ganciclovir again, that molecule can just as easily float back into the intestine or go on to be

absorbed. So just because we produced this inside the cell doesn't mean it gets into the body.

Can I have the next slide, please.

This is the bottom of the cell. So we have to go through this cell to reach the bloodstream. How does it get out of what we call the basolateral membrane? I don't know whether both of these can get through that membrane. It's highly unpredictable. And the next step converts it to ganciclovir.

So now, your Honor, you have a dilemma. You have a prodrug that must survive the intestine, may or may not survive the enterocytes; and if I design it so that it survives up here and up here, what's to say it is going to get converted in the body?

And so the balancing act of trying to design a prodrug that adequately delivers this drug ganciclovir into systemic circulation is a highly unpredictable convenient.

BY MR. VERDIRAME:

Q. And what happens if you succeed in all of these endeavors?

A. If you succeed in all of those endeavors, you have good oral bioavailability. The failure is not only that you didn't design the right molecule; if you expose the body to one or both of these materials, we

really don't know if they are going to be toxic or not. There is no way we can predict from a chemical structure whether any molecule we produce is going to be toxic or nontoxic.

Q. Can we please turn back to Exhibit PTX-1, the '953 patent.

Is there a place in the '953 patent which shows the oral bioavailability achieved by the vendors?

A. Yes, I believe it is in column 28, example 9.

Q. On the screen now is what you are referring to, Dr. Stella?

A. Yes, it is.

Q. Please explain what this Table 7 from the '953 patent in this case shows.

A. I would like you to focus on the bis-valine ester which shows that the bioavailability as reported here is 52 percent, and the ganciclovir valinate acetate and hydrochloride, which is valganciclovir, the bottom is valganciclovir which is at 98 percent.

I would like you to recognize, your Honor, that the bioavailability of the mono-ester is about 1.5, approximately two times better than the bis-valine ester.

MR. JENNINGS: Your Honor, I'm going to have

to object as outside the scope of the report. This particular data was not discussed in the report.

MR. VERDIRAME: Your Honor, these results were discussed in Dr. Stella's entire report. The oral bioavailability results achieved in the '953 patent is the subject of Dr. Stella's report.

MR. JENNINGS: It was discussed generically, your Honor. We went through the file history where the applicants acknowledged the error with respect to this data. We had no notice the expert would be now testifying in support of this data in their patent.

MR. VERDIRAME: This is the patent, your Honor. This is exactly what Dr. Stella was talking about in his report.

THE COURT: You would think so if that's what he is opining on.

You may continue.

BY MR. VERDIRAME:

Q. Does this data show good results for valganciclovir hydrochloride?

A. Yes, it does.

Q. Is there other information in the file history of the '953 patent that provides additional information about bioavailability of the compounds valganciclovir hydrochloride?

A. Yes. There is a declaration by Susan Malcolm.

MR. VERDIRAME: Please put up DX-10 at page 1148 on the screen.

Q. That's in the big binder in front of you, Dr. Stella.

A. Yes.

Q. Is this data from the Malcolm declaration you are referring to?

A. Yes, it is.

Q. What does this Table 7 show?

A. This Table 7 shows a study, that is what's called a side-by-side study, where the researcher, Susan Malcolm, determined the oral bioavailability of ganciclovir, what we call the parent drug. It has a bioavailability of 6.9 percent. The bis-valinate has a bioavailability of 34 percent. And valganciclovir has a bioavailability of 55.4 percent.

You'll notice, your Honor, the ratio of the bioavailability of the monovalinate to the bis-valinate is about the same as what was seen in the example 9 of the '953 patent.

Q. Are the bioavailability numbers in examples 9 and 10 of the '953 patent and the numbers in the Malcolm declaration the same?

A. No, they are slightly different.

Q. Please explain why.

A. First of all, the explanation for those differences was actually present in the Malcolm declaration. In the paragraph immediately following this Table 7 in the Malcolm declaration, it explains why there is a difference, I believe, the rat data that was in the '953 patent and the data that was in the Malcolm declaration.

Earlier, your Honor, I described how you perform an oral bioavailability assessment. In the oral bioavailability assessment, you remember I talked about determining the area under the curve intravenous versus oral. When doing a drug discovery process within a drug company, invariably what happens is very early, the researchers do the area under the curve or the plasma level time data for ganciclovir. If you run a control experiment, where you determine the plasma level of the intravenous ganciclovir, if one is comparing and determining absolute bioavailability, as is illustrated here in both the Malcolm declaration and the '953 patent example 9, a fair amount of error comes into the data because the ratios are largely determined by what the plasma level is from the IV data.

So when one compares and determines the

bioavailability over here, you are at the mercy of the quality of the data, the intravenous control data. And Malcolm, Dr. Malcolm -- I think it is Dr. Malcolm, Susan Malcolm, points out that in the data that was presented in the '953 patent, had an inadequacy in the control experiment -- that is, the intravenous ganciclovir data.

If you notice, I emphasized the ratio of the bioavailability from the valganciclovir, the bottom compound here in yellow and the bis derivative and that ratio was the same in the two studies. The absolute numbers were off. That was adequately described in the Malcolm declaration.

Q. Is it correct to say that the data in example 9 of the patent is in error?

A. No, it is not an error.

Q. Looking at the data that's on the screen in front of you, Dr. Stella, what is the oral bioavailability for ganciclovir?

A. The oral bioavailability of ganciclovir is 6.9.

Q. What is the oral bioavailability for ganciclovir bis-valinate hydrochloride?

A. 34 percent.

Q. What is the oral bioavailability for ganciclovir monovalinate hydrochloride?

A. It is 55 percent.
Q. And that's valganciclovir hydrochloride?
A. Yes.
Q. Are these results for ganciclovir monovalinate hydrochloride good results?
A. These are outstanding results in the rat model.
Q. Does this data for the ganciclovir monovalinate hydrochloride show results that would have been expected by persons skilled in the art in 1994?
A. No.
MR. VERDIRAME: Please put up DX-807.13 referred to by Dr. Sloan last week.
A. Yes.
Q. Were you here last week when Dr. Sloan referred to this slide, Dr. Stella?
A. Yes, I was.
Q. Dr. Sloan testified that the results achieved by the '953 patent allegedly were expected results. Was he correct?
A. No, he was not.
Q. Why not?
A. Very simply, he and the examiner both made the assumption that you can extrapolate the data from acyclovir to ganciclovir. These are two different molecules.

As I demonstrated in my lock and key example, small structural differences in the molecules can lead to big differences in the ability of those molecules to both interact with viruses, as we know in the case of the two compounds. We know ganciclovir is more toxic than acyclovir. And to assume that valganciclovir, a promoiety, would perform as well as acyclovir is a stretch of the imagination.

Both Sloan and the patent examiner inappropriately did not consider the improvement of the bis-valinate. And the bis-valinate is the only thing that I know that was in fact presented in the prior art. I think that the patent examiner inappropriately should have compared the improvement in the bioavailability of valganciclovir only to ganciclovir and the bis-valinate.

Q. Did the examiner ever evaluate that comparison?

A. No, they did not.

Q. In your testimony today, did you evaluate that comparison?

A. Yes, I did.

Q. Does the slide shown in front of you here today confirm that the examiner did not evaluate that comparison?

A. Yes.

If you look at the last sentence here, your Honor, "Hence, comparison with the bis-valinate does not establish patentability in this rejection.", I disagree with that.

Q. Did the file history show that the applicants continued to urge that the comparison should be with the bis-valinate?

A. Yes, they did. All through their file history they focused on and felt that what was important was that that the comparison to the bis-valinate was a critical element, and I think, stubbornly, the patent examiner focused on the comparison to acyclovir and valacyclovir. Those are different molecules. And as you can see, your Honor, the complexity in being able to deliver a prodrug like this is quite a challenge.

Q. Did the examiner ever say there was no unexpected results for the monovalinate as compared to the bis-valinate?

A. No, he did not.

Q. Do you recall Ranbaxy's counsel noted last week that the claims of the '953 patent covered individual diastereomers of valganciclovir?

A. Yes.

Q. Do the claims of the '953 patent also cover the mixture of the valganciclovir diastereomers?

A. Yes, it did.
Q. Was it pertinent to your analysis that the claims cover a mixture of diastereomers in crystalline form?
A. Yes.
Q. Why is that?
A. The reason for that is, one, as I think was adequately pointed out by Professor Mitscher, it was quite surprising and unexpected that the diastereomers in the hydrochloride formed a crystalline material. Diastereomers often do not co-crystallize or crystallize into a mixture.

Two is that the two diastereomers, the mixture, showed really superb oral bioavailability.
Q. Dr. Stella, having reviewed the '953 patent, the prosecution history, and the bioavailability results, do you have an opinion on the nonobviousness of the '953 patent?
A. I think the '953 patent was nonobvious.
Q. Could you please briefly summarize your reasons.
A. Well, first, the bioavailability of ganciclovir from valganciclovir is outstanding. The valganci-clovir is a diastereomer mixture, and, as such, would not be expected to readily crystallize, and would not be expected that the mixture would provide the superb

bioavailability that was observed in this case, and it also happens to be a great drug.

Q. Thank you.

MR. VERDIRAME: Your Honor, we have no further questions.

THE COURT: Are you moving in any exhibits?

MR. VERDIRAME: There is Exhibit 655, which is Dr. Stella's CV. We would like to move that into evidence.

Also, for demonstrative purposes, we would like to move into evidence PTX-683, which was the prodrug barrier diagram; demonstrative PTX-754, regarding the animation for prodrug delivery; and Exhibit 755, the lock and key exhibit.

MR. JENNINGS: No objection.

THE COURT: The one exhibit will be admitted in evidence, and the others will be noted as demonstratives.

(Plaintiff's Exhibit No. 655 was received in evidence.)

CROSS-EXAMINATION

BY MR. JENNINGS:

Q. Good morning, Dr. Stella.

A. Good morning.

MR. JENNINGS: If we could please have Dr. Stella's demonstrative slide 683, please.

Q. Now, Dr. Stella, using your demonstrative slide, I would like to review with you the observations about acyclovir and valacyclovir in relation to this slide. Okay?

A. Okay.

Q. In your binder you have the prior art among other exhibits. If you could turn to Defendant's Exhibit 170, please.

A. Yes.

Q. This is a paper where Dr. Beauchamp reports in 1992 her observations about valacyclovir. Correct?

A. That's correct.

Q. And first in relation to your slide here, acyclovir is the drug. Correct?

A. In the case of the Beauchamp paper, yes.

Q. Okay. And Dr. Beauchamp reports that the drug had limited oral bioavailability. Correct?

A. That's correct.

Q. Okay. And so to improve that bioavailability, Dr. Beauchamp made amino acid esters of that drug. Correct?

A. Yes, she made 18 esters.

Q. And she reported her observations about that in

her paper?
A. Yes.
Q. She determined that L amino acid esters were better. Correct?
A. That's correct.
Q. And she reported those observations. Correct?
A. Yes.
Q. And she determined that L-valine amino acid ester was the best. Correct?
A. She found that the L-valine provided the best oral bioavailability in the rat for this series of molecules.
Q. And she said in that exhibit clearly the L-valyl ester provided the best any acyclovir bioavailability which she reported as 63 percent. Correct?
A. Yes.
Q. And she reported that observation, and she also reported that on the other side of your barrier that prodrug was very quickly and effectively hydrolyzed. Is that correct?
A. That's correct.
Q. By "hydrolyzed" on your right side of your slide it is transform or broken apart, so you have the separate the promoiety from the drug. Correct?
A. That's correct.

Q. In fact, if you could turn to Defendant's Exhibit 170 at page 4, she says--
A. Page 160 of the paper?
Q. Yes. And in the paragraph just before "aqueous solubility," she says:

"Prodrug was undetectable one hour post dose."

Do you see that?
A. Yes.
Q. That means she's reporting that one hour post dose you can't find any more of the prodrug. That's the L-valine connected to the acyclovir. Correct?
A. That's correct.
Q. It's been separated?
A. Yes.
Q. That's the highly efficient hydrolysis. Correct?
A. Yes.
Q. And the examiner, of course -- you have been here and you listened to us discuss the file history?
A. Yes.
Q. The examiner said he viewed the prior art and determined in his view one of skill in the art would consider ganciclovir and acyclovir extremely similar. Correct?

A. That's what he said. I disagree with him.
Q. Those two compounds have similar uses. Correct?
A. They are used for herpes infections. One is superior for the treatment of general warts, et cetera, and herpes simplex, while ganciclovir is primarily used for treatment of CMV.
Q. So both are used to treat viruses in the herpes family. Correct?
A. That's correct.
Q. In fact, ganciclovir was reported in the Martin paper as a potent and broadly active anti-herpes agent. Do you agree with that?
A. Yes. It is also fairly toxic.
Q. Okay. And acyclovir and ganciclovir are both known to have that problem that we talked about, the low oral bioavailability. Correct?
A. Yes.
Q. And so these known potent anti-herpes agents had the same need, improve their oral bioavailability. Correct?
A. That is correct.
Q. And we have just gone through what Dr. Beauchamp's observations were with respect to valacyclovir. Correct?
A. Yes.

Q. So you would agree that these observations for valacyclovir influenced the development of valganciclovir. Correct?
A. I believe it restarted activity at Roche to assess improving the bioavailability of ganciclovir.
Q. So you would agree, then, that the observations in the prior art about valacyclovir did in fact influence the development of valganciclovir?
A. They influenced it, but it really just restarted the program to evaluate what would work with ganciclovir because one would know that what was applicable to acyclovir may not be applicable to ganciclovir because of the structural differences.
Q. Dr. Stella, are you familiar with the book "Optimizing the Drug-Like Properties of Leads in Drug Discoveries"?
A. Yes.
Q. In fact, you wrote a chapter in this book, "Optimizing the Drug-Like Properties of Leads in Drug Discoveries"?
A. Yes.
Q. And you wrote Chapter 10?
A. Yes.
Q. Would you like a copy?
A. I would like to have another copy for my

library.
Q. This is your chapter?
A. Yes, it is.
Q. In we could turn to page 231, the last paragraph, you state in the last paragraph of your book:

"Valacyclovir is an example where lady luck plays a role."

And you illustrate the role that serendipity plays in the drug discovery process:

"Is the choice of L-valine esters one that someone would make from first principles? It is unlikely, but the discovery and development of valganciclovir was influenced by the observations made with valacyclovir."

You wrote that. Correct?
A. Yes. I just told you I didn't disagree with that. I said that clearly the appearance of the Beauchamp papers reenergized an interest in looking at prodrugs of ganciclovir.
Q. So you referred to "serendipity" with respect to valacyclovir, but that discovery influenced valganciclovir. Correct?
A. To restart a program, yes.

Q. You didn't say that --
A. I did, "influence the observations made by valacyclovir."
Q. You didn't say "restart a program"?
A. Well, it's semantics, sir.
Q. Okay. Now, you agree that in Beauchamp's '339 patent she describes prodrugs for ganciclovir?
A. Amongst many others, yes.
Q. That patent is Exhibit 101 in your binder.
A. Yes.
MR. JENNINGS: Now, if we could have Dr. Stella's demonstrative Exhibit 683 up again.
Q. Now, I'd like to review with you, sir, what's reported about ganciclovir in DX-101 and how it relates to your demonstrative slide.
So we first have the drug which is ganciclovir on the left side. Correct?
A. Correct.
Q. And the patent states that "ganciclovir has low oral bioavailability" in column 1, lines 21 and 22. Correct?
A. Yes.
Q. And in the fifth paragraph --
A. Where is that -- excuse me while I read this, please?

(Pause.)

Yes, it does.

Q. In column 1 there is a whole paragraph discussing ganciclovir?

A. Yes. And a number of other derivatives.

Q. And the ganciclovir compound is discussed in the paragraph from lines 14 down to 24. Correct?

A. Yes, it does.

Q. In the fifth paragraph, the '339 patent states:

"We have now found that amino acid esters of the compounds referred to above surprisingly have advantageous bioavailability when administered by the oral route resulting in exceptionally high levels of the parent compound in the body."

I read that correctly?

A. Yes.

Can I make a comment about that, please?

Q. Did I read that correctly?

A. Yes.

Q. And ganciclovir was one of the compounds referred to above that paragraph 5 in column 1 of Beauchamp's '339 patent. Correct?

A. Yes.

Q. So in relation to your slide, we had ganciclovir on the left, and that's the drug that doesn't get through the barrier well; and then we have in paragraph 5 of Beauchamp's paper, she reports that amino acid esters of the compounds referred to above, which include ganciclovir, have advantageous bioavail-ability when administered by the oral route.

So that means they are getting through the barrier. Is that correct, sir?

A. That is correct.

However, you heard my earlier discussion about how to assess oral bioavailability. One cannot do oral bioavailability without having made the compound and experimentally determining it. There is nothing in the '339 patent on the mono or the valine ganciclovir. The only compounds that are mentioned in the '339 patent that are made, and you can only assess bioavailability if the compounds are made, is --

THE COURT: Let me just stop you. You are really critiquing what you explained. I'll just ask you, on cross-examination, listen to the questions and respond to what they are. I think you did answer it, "That is correct," and the "however," really, is not applicable.

I'll strike that part.

Q. So the oral bioavailability means if you take her at her word, it's getting through your barrier. Correct?

A. Yes.

Q. And she goes on, and she refers to "exception-ally high levels of the parent compound in the body" in that same sentence. Correct?

A. That is correct.

Q. So what that tells you, if you take her at her word, is you are getting transformation on the right side of the body so you have high levels of the drug ganciclovir. Correct?

A. Taking her at her word, yes.

Q. I would like to turn back for a moment to Dr. Beauchamp's paper regarding valacyclovir. This is Exhibit 170.

A. I have it.

Q. You mentioned this on direct examination about the amino acid portion of the valganciclovir molecule. I would like to talk about it with respect to what Beauchamp says in relation to valacyclovir.

She states on the bottom, towards the bottom in the paragraph under discussion on page 5:

"On the other hand, the stereo-chemistry of the amino acid in the

prodrug esters had a marked effect on absorbtion."

She states that?

A. Yes.

Q. You agree here she refers to the stereochemistry of the amino acid in this sentence of her paper. Correct?

A. Yes.

Q. And you agree she found that L amino acids were best. Correct?

A. Yes.

Q. If we continue on at page 5 in the sentence bridging column 1 and column 2 she states:

"The preference for the L versus D isomer, and for the naturally occurring branched chain amino acids L-valyl and L-isoleucyl suggests that a stereospecific transporter may contribute to the improved absorption of these esters."

Again, she's referring to the stereochemistry of the amino acids she adding. Correct?

A. Yes.

Q. And if you could turn to her 1993 paper.

MR. JENNINGS: This is Defendant's Exhibit

171, please.

Q. She addresses this same issue. Page 9 of the exhibit.

Do you have that before you?

A. Yes.

Q. So her 1993 paper, Dr. Beauchamp states:

"The structure activity relationship of the amino acid esters suggests the involvement of a stereospecific L versus D transport process. The common branched chain amino acids, L-valine and L isoleucine, are favored by this proposed transporter."

Again, she's referring to the stereochemistry of the amino acid she's adding to make the ester for her prodrugs. Correct?

A. Yes.

Q. Now, do you agree that the patent examiner found that it was the amino acid that was responsible for the improved bioavailability in the valacyclovir publications?

A. The patent examiner I think was a little naive on this. There is no question I think that the L-valine esters clearly contributed to the adequacy of

the transport. But, as I mentioned earlier, it is not just the L-valine; it is what it is connected to. The whole molecule is transported, and the L-valine and L esters play a very important role.

THE COURT: The question was -- he asked: What did the patent examiner find?

THE WITNESS: And I disagreed.

THE COURT: So the answer to the question was --

THE WITNESS: I said: "Yes." I meant to say: Yes, the patent examiner did agree on that, but I thought the examiner was naive on the total package.

BY MR. JENNINGS:

Q. So you do agree the examiner found that it was the amino acid that was responsible for the improved absorption?

A. Yes, but I can disagree with him.

Q. Well, in fact, Dr. Stella, in your report, and that's in the beginning of our binder that we provided up to you, you did refer to the examiner in paragraph 127 of your report.

Let me read what you said in your report:

"My conclusion is bolstered by the fact that the examiner of the '953 patent had essentially the same prior

art references before him and also disagreed that these references rendered the claims unpatentable."

Now, in your report, you took stock with the examiner's view, you said here. Correct?

A. I took stock with the examiner's view that valganciclovir hydrochloride in crystalline form was patentable.

Q. But the examiner never agreed that valganciclovir itself was patentable. Correct?

A. In what way?

Q. The examiner never agreed valganciclovir was patentable. Correct?

A. No, he did not. The examiner did not allow valganciclovir per se to be patentable.

Q. And the examiner also, over and over again, refused to allow the compound valganciclovir hydrochloride. Correct?

A. He refused to allow -- I don't agree with that decision.

Q. And the examiner only ultimately allowed a patent here when it was narrowed to the specific crystalline form, and the declarations we discussed here at trial were submitted. Correct?

A. Yes.

Q. You have offered no opinion about those declarations and the crystallinity issues in those declarations. Correct?
A. In my report I talked about the importance of crystallinity but not as it relates to the patent, I don't believe.
Q. And you referred to -- well, in fact, do you agree the examiner rejected the opinion you presented here today that the key was unknown from the prior art?
A. I don't understand your question.
Q. Well, you said something about Dr. Sloan stealing your thunder?
A. Yes.
Q. By the way, Dr. Sloan is a co-inventor with you on that phenytoin product?
A. That's correct. We are still good friends even after that.
Q. And this is in the big binder. It's down to your left in the big box, Defendant's Exhibit 10. This is the prosecution history?
A. Yes.
Q. This is Defendant's Exhibit 10 at 1032.
A. Yes.
Q. In the file history here, the examiner states:

"Thus, it is clear that the key is getting the right amino acid to interact with the stereospecific transporter and being the sort of amino acid which is efficiently enzymatically hydrolyzed, 'but for a grammar issue, the examiner found that the key in the examiner's view, the key was, one, getting the right amino acid to interact with the stereo-specific transporter, and, two, that amino acid being the sort that is efficiently enzymatically hydrolyzed.'"

Correct?

A. That is correct for acyclovir.

Q. And valganciclovir uses the same amino acid as valacyclovir. Correct?

A. After extensive experimentation, yes.

Q. So now we have this ganciclovir, which was a broadly active anti-herpes agent with a particular activity against CMV; and is it your opinion that after Dr. Beauchamp discovered that L-valine ester of acyclovir gave the huge improvement in the bioavaila-bility of acyclovir, one of ordinary skill in the art

would not even try a mono-L-valine ester of ganciclovir?

A. One would start a research program to explore the ability to deliver the drug through the use of amino acid esters.

Q. So do you agree with me, then, sir, that given the huge improvement that Beauchamp reported from making an L-valine amino acid ester of acyclovir, that one of skill in the art would have been motivated to try the mono-L-valine ester for ganciclovir to improve its oral bioavailability?

A. One would have been motivated to make the bis-ester based on what was taught by both the '92 paper, the '93 paper, and '339 paper.

Q. I'm going to go back to my question. Agree with it or disagree with it.

Is it your opinion that after Dr. Beauchamp discovered that the L-valine ester of acyclovir gave this huge improvement in bioavailability and reported those results, that one of ordinary skill in the art would not even try a mono-L-valine ester for ganciclovir?

A. One would not even try? No.

Q. So you agree one would try?

A. No, they would not try.

Q. I understand your position then.

In PTX-754, you went through your slide on the board. You raised a lot of questions about bioavailability?

A. Yes.

Q. And whether you might ever get the drug in the body?

A. That's correct.

Q. But if one simply takes Beauchamp at her word in the '339 patent when she said in that U.S. patent that her amino acid esters of ganciclovir had advantageous bioavailability when administered by the oral route resulting in exceptionally high levels of the parent compound in the body, then we would have no question about whether we are going to get high levels of the parent compound in the body for those amino acid esters. Correct?

A. The bioavailability referred to there must be a reference to the bis-ester.

Q. She doesn't say that in the sentence that I just quoted from paragraph 5 of column 1. Correct?

A. That's what she states. Am I allowed to do a "however"?

THE COURT: I'm not sure what you are saying she does state. I'm not sure what your answer just

referred to.

Maybe we better go back. Ask a question again.

Q. Let's go to the document then.

We went through column 1, and we agreed that in the third paragraph she talks about ganciclovir. Correct?

A. Yes.

Q. And then in the first sentence of the fifth paragraph, she says:

> "We have now found that amino acid esters of the compounds referred to above surprisingly have advantageous bioavailability when administered by the oral route resulting in exceptionally high levels of the parent compound in the body."

What I'm asking you is: If you take her at her word here -- we don't have the questions that you raised in PTX-754. She is telling us we are going to get high levels of the parent compound in the body with the amino acid esters of ganciclovir. Correct?

A. That's what she says, but I disagree with the generality you are using here.

Q. We have talked about some data for amino acid

esters for ganciclovir. Correct?
A. You mean from the '953 patent and the Malcolm declaration?
Q. You talk about some data. Correct?
A. Yes.
Q. You do recall the applicants acknowledged there were errors with respect to the data in their patent. Correct?
A. They acknowledged there was inadequacy the way the data was evaluated.
Q. And they submitted a declaration to -- in fact, they expressly explicitly withdrew any reliance on the data in the patent; didn't they?
A. That's because --
THE COURT: Just answer the question.
THE WITNESS: Sorry.
Q. They explicitly withdrew any reliance on the data in the patent. Correct?
A. I believe they -- I don't remember reading -- I remember reading, but I don't remember the exact language. So I don't know if it is consistent with what you just said.
MR. JENNINGS: That language is available for the Court.
Q. If we talk about the data that was submitted in

the declaration, we have data for two amino acid esters of ganciclovir. Correct?

A. Yes.

Q. And we have the bis-valine ester. Correct?

A. That's correct.

Q. That was a five-fold increase over ganciclovir. Correct?

A. Yes it was.

Q. So that's consistent with what Beauchamp says right here in paragraph 5 of column 1 of her patent. Correct?

A. That is correct.

Q. And we also have data for the mono-L-valine ester. Correct?

A. In the Malcolm declaration.

Q. Yes.

A. Not in the '339 patent.

Q. Okay. And we have that data. Correct?

A. Yes.

Q. And that data is also consistent with what Beauchamp says in column 5 of her '339 patent. Correct?

A. Yes, and she could not have determined that because she never made it.

Q. You have no personal knowledge of what

Dr. Beauchamp actually did. Correct?
A. How can I have knowledge of what Dr. Beauchamp did. I can only go on what's in the '339 patent.
Q. You just testified what she did. You have no personal knowledge?
A. No, I have no personal knowledge.
Q. She says you are going to get this improved bioavailability and exceptionally high levels of the parent compound in the body, and we have data for two examples of amino acids of ganciclovir, and her statement holds true for each of them. Correct?
A. Only for those -- yes, only holds true for those she made.
Q. Her statement in paragraph 5, column 1, holds true for each of the amino acid esters of ganciclovir for which we have looked at data. Correct?
A. She doesn't present any data -- sorry. You are referring to the Malcolm declaration?
Q. Yes.
A. Say it again. I was thinking you were referring to the '339 patent.
Q. She has a statement in her '339 patent that says you are going to have improved oral bioavailability and exceptionally high levels of the parent compound in the body for amino acid esters of ganciclovir.

Correct?

A. She said that, and she could not have done the mono-ester.

MR. VERDIRAME: Objection.

Q. But she says that. Correct?

A. She says that.

Q. And sitting here today, we have looked at two amino acid esters of ganciclovir. Correct?

A. Again, are you referring to the Malcolm?

Q. Yes. Correct?

A. Yes.

Q. And that data is consistent with what Beauchamp says one gets with the amino acid esters of ganciclovir. Correct?

A. That's an outstanding result.

Q. And you haven't referred us to any data -- strike that.

There are four amino acid esters mentioned by name -- strike that.

There are four amino acids referenced by name in Beauchamp's '339 patent. Correct?

A. Yes. And the preferred number is actually 14.

Q. There are four amino acids mentioned by name in the '339 patent. Correct?

A. That's correct.

Q. And valine is one of the four?
A. Yes.
Q. And we reviewed data for valine both as a bis ester and mono-ester. Correct?
A. Yes.
Q. And both have improved bioavailability, and you haven't pointed us to any data for any of the other three that did not conform to what Beauchamp says in paragraph 5 of column 1. Correct?
A. Could you restate that, please?
Q. We have improved bioavailability for both of the valine esters of ganciclovir, and you have not pointed us to any data for any of the other three that she names in her '339 patent where her statement in paragraph 5 is not correct?

MR. VERDIRAME: Your Honor, I object to this question. Counsel is trying to rewrite the '339 patent by including information from the Malcolm declaration into the patent which is not there.

THE COURT: It is not clear to me at all that's what he is doing, and I'm going to let him probe this. He is probing this expert's opinions.

THE WITNESS: It's been a while since I read the '339 patent.

THE COURT: Why don't you direct him to the

portion of it you would like him to look at.

Are you going to be awhile, Mr. Jennings?

MR. JENNINGS: Could be 15 minutes.

THE COURT: Let's take a break for a moment, and you can bring him back in the patent.

You may step down.

(Witness temporarily excused.)

THE CLERK: All rise.

(Recess.)

(Continued on the next page.)

///

(In open court.)

THE CLERK: All rise.

THE COURT: Thank you. Everyone may be seated.

Thank you. Mr. Jennings, you may proceed

VALENTINO J. STELLA, resumed.

CROSS-EXAMINATION (continued)

BY MR. JENNINGS:

Q. Dr. Stella, we were discussing Beauchamp's '339 patent which is DX-101 in your binder.

I would like to draw your attention to the paragraph on column 2 starting at about line 17. Do you see these four amino acids referred to by name: glycine, alanine, valine, and isoleucine?

A. Yes.

Q. The preference for the L amino acid is also stated here in this paragraph?

A. Yes.

Q. And for esters with these four amino acids, have you seen any data inconsistent with the statement in the first sentence of paragraph 5 of column 1 -- and I'll read you that sentence:

"We have now found that amino

acid esters of the compounds referred to above surprisingly have advantageous bioavailability when administered by the oral route resulting in exceptionally high levels of the parent compound in the body."

A. I would like to go back and just read the information on column 1 just to make sure I fully understand the context.

Q. The context is this sentence here in paragraph 5 of column 1, and with respect to that first sentence of paragraph 5 of column 1, would you agree --

A. What I want to do is look at what is said about amino acid esters in column 1. So I just want to refresh my memory on that.

Will you hold off for a minute while I read that again?

THE COURT: The question mentions the compounds referred to above.

THE WITNESS: I just want to read that for one second.

(Pause.)

A. Yes.

Q. You have that sentence in mind?

A. Yes.

Q. And valganciclovir is one of the compounds referred to above. Correct?
A. That's correct.
Q. With respect to the amino acids glycine, alanine, valine, and isoleucine, we have seen no data inconsistent with the statement in paragraph 5, first sentence. Correct?
A. No. Can I go back to that?
Q. We have seen no data inconsistent with this statement?
A. No. The only data that I want to --
Q. It's just not clear. When I say we have seen no data inconsistent, is that a correct statement?
A. Yes.
Q. Now, you will agree -- we have to take -- that's the rule here. We have to take Dr. Beauchamp for what she says at face value. Correct?
A. On the bioavailability, yes.
Q. So you agree that's the rules here, we take her at face value when she says she discovered "advantageous bioavailability when administered by the oral route resulting in exceptionally high levels of the parent compound in the body"?
A. I have to take her at her word, but she can only support that with the data on compounds she made, and

the only compounds that are shown here in the examples 1 through 6, not all of them are ganciclovir, are compounds related to the bis-esters.

So that bioavailability statement could not be asserted to mono-esters because they were never made and tested.

Q. Let's look at what the examiner said with respect to the rules taking Dr. Beauchamp at her word in her U.S. patent.

If you could turn, please, to Defendant's Exhibit 10 -- this is the big binder -- at page 1037, the examiner stated:

> "This is a U.S. patent, and what it says is taken at face value unless persuasive reasons are presented to show that the statements are inaccurate. That has not been done here. Applicants have made no attempt to show inaccuracy but, instead, try to read the reference as if there were no teaching that mono-esters are useful for this utility."

That's what the examiner said. Correct?

A. That's what the examiner said.

Q. And you today are trying to read the reference as if there is no teaching that mono-esters are useful for this utility. That's how you are trying to read the reference today. Is that correct?

A. All I am saying is the reference to bioavaila-bility that was in the '339 patent could not have been to a mono-ester because the mono-esters were never made. Bioavailability of the mono-esters were never assessed because to assess them you would have had to make them, and they were never made.

My feeling, my expert opinion is that you cannot read into bioavailability in that statement that you are referring to, to the mono-esters, because they were never made and, therefore, could not have been determined.

Q. You have no personal knowledge as to what was ever made. Your statement is based entirely on the fact there was not an example specifically making the mono-ester in the patent. But you have no personal knowledge that Dr. Beauchamp never made a mono-ester. Correct?

A. No, I do not know that Dr. Beauchamp made a mono-ester.

Q. Now, will you agree that the named vendors of the '953 patent identified valganciclovir as the lead

prodrug for ganciclovir using the same prodrug approach as that for acyclovir?

A. The patent defines valganciclovir hydrochloride in crystalline form, and that's what they are claiming.

Q. Do you agree that the named vendors of the '953 patent identified valganciclovir as the lead prodrug for ganciclovir using the same prodrug approach as that for acyclovir?

A. If they used the same approach for ganciclovir as they used for acyclovir, they would have made the bis-esters.

Q. So you disagree with my statement?

A. Yes.

Q. Could you please turn to the exhibit marked 809 for identification in your binder. It is excerpts from the Journal of Pharmaceutical Sciences.

A. Yes.

Q. You are familiar with the Journal of Pharmaceutical Sciences?

A. Yes, I am.

Q. Are you part of the editorial board?

A. Yes, I am.

Q. Could you please turn to page 1109 of the journal. Do you have that before you?

A. Yes.
Q. This is an article titled "Prodrugs of Nucleoside Analogues for Improved Oral Absorption and Tissue Targeting." Did I read that correctly?
A. Yes.
Q. One of the authors is Hans Maag, one of the named vendors of the '953 patent. Is that correct?
A. That's correct.
Q. And the article identifies him as a member of the Department of Medicinal Chemistry, Roche Palo Alto, LLC. Correct?
A. Yes.
Q. Could you please turn to page 1114 of the journal article.

Do you see in the bottom right-hand section of Dr. Maag's article there is a title, "Acyclovir and Valacyclovir"?
A. Yes.
Q. Could you please turn to page 1116 of the article.

The next section is titled, "Ganciclovir and Valganciclovir." Correct?
A. Yes.
Q. And the first sentence of that sentence states:

"Ganciclovir structurally similar to acyclovir but differing from the latter by the addition of a hydroxymethyl group to the side chain is also active against HSV and cytomegalovirus CMV."

Did I read that correctly?

A. Yes.

Q. HSV is herpes simplex virus. Correct?

A. That's correct.

Q. Could you please turn to page 117.

A. Yes.

Q. The first sentence of the first full paragraph on the left-hand column states:

"Using the same prodrug approach as that for acyclovir, the valine ester of ganciclovir (valganciclovir) was identified as the lead prodrug based on marked increase in oral bioavailability."

Did I read that correctly?

A. That's correct.

Q. That's what the inventor said about the identification of valganciclovir as the lead prodrug. Correct?

A. That was in 2008.
Q. Is that what the inventor said --
A. Yes, that was in 2008, and that's hindsight.
THE COURT: All you need to do is answer the question. If they want to follow up on something on redirect, they may.
Q. That's what the inventor said. Correct?
A. Yes.
Q. The inventor said he used the same prodrug approach. Correct?
A. That is correct.
MR. JENNINGS: Thank you, sir. No further questions.
THE COURT: Mr. Verdirame.

REDIRECT EXAMINATION
BY MR. VERDIRAME:
Q. Dr. Stella, please keep that publication in front of you. DX-809.
That's still in front of you?
A. Yes.
Q. Counsel just asked you about page 117 of that publication?
A. Yes.
Q. Could you please turn to page 116 right before

it, and the second column towards the middle of the bottom right-hand paragraph --

MR. JENNINGS: Hearsay, your Honor.

THE COURT: Are we looking at Dr. Maag's --

MR. VERDIRAME: The same publication, yes.

MR. JENNINGS: Objection; hearsay.

THE COURT: He is not offering it for the truth. You asked him about the document, whether he agrees with it. Let me hear the question.

BY MR. VERDIRAME:

Q. Dr. Stella, do you see in the middle of the paragraph on the right, on the bottom, the publication says:

"Prodrugs approaches were applied to improve oral bioavaila-bility of ganciclovir."

Do you see that?

A. Yes.

MR. VERDIRAME: I have no further questions, your Honor.

THE COURT: All right. Thank you.

MR. JENNINGS: Your Honor, it's hearsay. It's a party offering their own statement out of court.

THE COURT: I don't have the document before me. Let me see what it is. Is it a declaration? Is

it a publication?

MR. VERDIRAME: Publication.

THE COURT: You asked him about what was said in the publication. The whole publication is hearsay. The questions that you asked him about, what went on, I haven't heard him say that he'd actually done. I'm not admitting it for the truth. It was written there.

MR. JENNINGS: It was an admission for a party opponent.

THE COURT: I'm not admitting it for the truth of the statement that's indeed what he did in the study.

MR. JENNINGS: I'm using it to impeach the expert witness' testimony that they did not apply the same prodrug approach. An admission of a party opponent is admissible to impeach the expert testimony of Dr. Stella.

THE COURT: What is the purpose for which you are admitting this statement?

MR. VERDIRAME: Counsel had focused on one part of the prodrug.

THE COURT: Dr. Maag is coming. Let's wait and have him do it. I'll strike that, and you can bring it up with him.

MR. VERDIRAME: Very well.

THE COURT: Thank you, Dr. Stella. You are excused.

(Witness excused.)

MR. PEZZANO: Your Honor, our next witness will be Dr. Hans Maag. He is the vendor of Roche's patent No. 6083953, the '953 patent in suit.

He is currently the Vice President and deputy head of chemistry of plaintiff, Roche Palo Alto, LLC, and has been employed by Roche and its predecessor company Syntex U.S.A., Inc., since 1975.

Dr. Maag will lay a foundation for the powder X-ray diffraction analysis in June 1994 of the crystalline valganciclovir hydrochloride embodiment of the claimed invention shown in PTX-255 A.

HANS MAAG, called as a witness on behalf of the plaintiff, having been first duly sworn, testified as follows:

DIRECT EXAMINATION

BY MR. PEZZANO:

Q. Dr. Maag, please state your home address for the record.

A. My address is 442 Saul Saleto Boulevard in Saul Saleto, California.

Q. Are you currently employed?
A. I'm employed by Roche Palo Alto.
Q. What is your current title?
A. My current title is Vice President of Chemistry and Deputy Head of Chemistry in Palo Alto.
Q. How long have you held those positions?
A. I became Vice President in 2001 and Deputy Head in 2003.
Q. When did you begin your employment with Roche?
A. I started my career at Roche in New Jersey in 1975. I moved to Syntex in Palo Alto in 1985, and Syntex was acquired by Roche in 1995.
Q. So you left Roche and then landed back at Roche?
A. Yes, that's correct.
Q. Approximately when was the Roche acquisition of Syntex?
A. The acquisition of Syntex happened in 1995. It was completed in 1995.
Q. While you were at Syntex before the acquisition, what type of work did you do?
A. Through my career industry, I always worked as a medicinal chemist in all locations.
Q. Including Roche?
A. Including Roche.
Q. For purposes of facilitating your testimony here

today, do you understand that the reference to Roche includes the predecessor Syntex?

A. I understand that.

Q. Can you summarize chronologically your educational background.

A. I received my undergraduate training at the Federal Institute of Technology in Zurich, Switzerland, and finished the undergraduate studies with what we call a diploma, which is roughly equivalent to a Bachelor of Science in the U.S.. I continued at that institute for graduate studies and received a doctorate in science and technology which is roughly equivalent to a Ph.D. in this country.

Q. And was your doctorate degree in organic chemistry?

A. My degree is in organic chemistry, particularly in synthetic chemistry.

Q. I would like to direct your attention now to Plaintiff's Exhibit No. 1. It's on the screen.

Are you aware the '953 patent is the subject of this lawsuit?

A. Yes.

Q. And are you an inventor of the claimed invention of this patent?

A. Yes. I'm an inventor on this patent.

Q. If you turn in the patent to column 30. There are six claims listed there. You can look in your binder in front of you.

Are you one of the vendors of the subject matter of these claims?

A. Yes, I am.

Q. Who are your co-vendors?

A. John Nestor, Scott Womble, Paul Fatheree and Charles Dvorak.

Q. Now, I would like to direct your attention to PTX-255 A. That's in your binder, and we will show it on the screen as well.

Have you seen this powder X-ray diffraction analysis before?

A. Yes, I have.

Q. At the top of the page of the powder X-ray diffraction analysis what is the No. 18951-142-60?

A. This number indicates the sample as referenced by a notebook. The notebook is 18951 and the page is 142.

Q. Now, I would like to direct your attention to the next exhibit which is also in your binder, PTX-255 B.

What is shown here in PTX-255 B?

A. On this exhibit is a copy of a log book held in

the Analytical Department listing the experiments done with a particular instrument.

Q. What is the log book that you are referring to?

A. The log book shows the experiment being done on an XRD powder diffraction equipment.

Q. Does this log book also include analyses you have requested from the Analytical Department?

A. This log book has on the top line an entry which refers to valganciclovir hydrochloride, and I do not recall the exact circumstances. I was leading that effort at the time. So, indirectly, I must have requested this analysis.

Q. Does the log book entry that you referred to correspond to -- does the log book entry that you been referred to on PTX-255 B correspond to PTX-255 A X-ray powder diffraction analysis?

A. The top line refers to the same sample as is in PTX-255 A. The connection is through the lab notebook reference, 18951-142-60, as well as through the file name and the lab reference number, which is 086644.

Q. And on the log book entry, what is the date that is shown here?

A. The log book entry is June 1994. On this copy, unfortunately, one digit is cut off. I would estimate it is possibly June 10th, 1994.

Q. Why do you estimate it is June 10, 1994?
A. Because one can see a zero, and the sample which was reference sample, which was referenced here, was prepared June 2nd, 1994. Also, to add, lower down in this log book is a date of June 17th. So the top line has to be before June 17th, and, therefore, it is likely June 10th, 1994.
Q. What is the significance of that date "June 10" or "June 1994"?
A. It clearly demonstrates that this material was analyzed very soon after it was prepared in June 1994.
Q. Who was the analytical chemist for this material identified on the log book entry?
A. The analytical chemist analyzing the sample is Larry Norder.
Q. Who is Larry Norder?
A. He, at that time, was employed as an analytical chemist at Syntex.
Q. Now, turning back to the powder X-ray diffraction analysis, PTX-255 A?
In the upper left-hand corner of this powder X-ray diffraction analysis there is a date June 23, 2004. Do you see that?
A. Yes.
Q. What is that date?

A. That date is an error. It does not correspond to the log book entry, nor, to my understanding, when the sample was actually recorded.

Q. What should that date be?

A. The date should be June 10th, 1994.

Q. If you turn to PTX-255 C now, these are three laboratory notebook pages bearing Bates numbers R0315573 through 75. Have you seen these before?

A. Yes, I have.

Q. Who is the author of these laboratory notebook pages?

A. These are notebook pages from the work of Paul Fatheree.

Q. What is shown on these pages?

A. These pages show the first experiments to prepare valganciclovir hydrochloride, and this particular page details the hydroxynation step to remove the protecting groups.

Q. If you turn to the next page, what is shown on the second page, which is Bates No. RO315574?

A. The second page shows the continuation, and, in particular, the crystallization of 1 gram of the material obtained on the previous page.

Q. What is the designation of that material that you are referring to?

A. The designation of 0.65 grams of crystals as the lab notebook reference 18951-1-42-60.

Q. Is that the lab notebook entry that matches up with the X-ray powder diffraction pattern shown on PTX-255 A and the log book PTX-255 B?

A. Yes, these numbers match.

Q. Now, what is shown on the third page of this document, the third laboratory notebook page, RO315574?

A. The third page shows an almost identical experiment as on the first page except on a somewhat larger scale.

Q. Now, I would like to direct your attention to the '953 patent, which is Exhibit 1. Is the work that is disclosed on these laboratory notebook pages R0315573 through 75 on PTX-255 C disclosed in the '953 patent?

A. In the patent it's not exactly the same experiment. The experiment in example 3 was conducted on a larger scale. But in terms of the transformation and the way of isolation, it is essentially identical.

Q. Let's turn back to those laboratory notebook pages again shown in PTX-255 CA.

What was your role in the work in connection with those laboratory notebook pages?

A. At that time I directed the prodrug effort for ganciclovir, and in my role, I directed Paul Fatheree to conduct these experiments.

Q. And did he report this work to you?

A. He reported the results to me on essentially a daily basis. Most communications were done verbally. And I certainly visited his lab very frequently.

Q. Now, turning back to the second page of PTX-255 C, and the sample you have identified by the designation 18951-142-60, what was the date this sample was obtained?

A. The date associated with this sample is June 2nd, 1994.

Q. What is the compound that is the subject of this sample?

A. The compound is valganciclovir hydrochloride.

Q. What is the date that Paul Fatheree signed this laboratory notebook page?

A. He signed it on June 23, 1994.

Q. And was this sample the subject of the powder X-ray diffraction pattern shown on PTX-255 A?

A. Yes.

Q. Now, I would like to direct your attention -- let's turn to that powder X-ray diffraction again, PTX-255 A.

There is a number at the top RS79070-294. Do you see that?

A. Yes.

Q. If you turn to PTX-255 B on the log book entry, is the same number written down under the heading compound 79070-294?

A. Yes.

Q. And that's in handwriting on the log book entry. Correct?

A. Correct.

Q. Is it fair to say that handwritten entry was later typed onto the X-ray powder diffraction pattern PTX-255 A?

A. Yes, that's likely the event.

Q. Now, is that an accurate identifier for the sample that is the subject of the X-ray powder diffraction pattern in PTX-255 A?

A. It is not absolutely correct in that the first five digits, 79070, designate the compound which is valganciclovir. However, 294 would be used for acidic acid salt, whereas for the hydrochloride, what was supposed to be used is 194. We had at that time at Syntex a very rather complex numbering system.

MR. PEZZANO: I have no further questions, your Honor.

I would like to offer into evidence Plaintiff's Exhibits 255 A, 255 B, and 255 C.

MR. OLSON: Your Honor, 255 A is already in evidence. We object to the introduction of 255 B, which is apparently an XRD log book, which this witness would have no personal familiarity with, nor would he have prepared this. He is basically giving his 14-year after-the-fact assessment what he believes now, without any personal knowledge, with respect to what actually occurred. He is trying to explain away dates he says are in error on the scan and designations for the different salts than what he says now is the case, the hydrochloride salt.

And with respect to 255 C, this, of course, is not his notebook. He indicated in his testimony he verbally communicated primarily with Fatheree; and, in addition, we were never provided with Mr. Fatheree's entire notebook. They indicated during discovery that they tried to locate it and could not. So we were provided with literally a handful of pages of the notebook. I'm not suggesting it exists somewhere. They just can't find it. They tried. They couldn't produce it. And what the witness is doing, he is making assumptions that certain things are correct on these documents and certain things are incorrect when

it could be just the reverse.

What he's assuming are errors might be accurate, and what he is assuming is correct might be inaccurate, and he doesn't know because he is just giving us his present day assessment of these documents, which he had no direct involvement in. He is not knowledgeable about XRD scans or patterns. He left that up to the Analytical Department. He is not part of that department and never has been.

THE COURT: Mr. Pezzano, let's take them one document at a time. 255 B first.

MR. PEZZANO: 255 B, that's the log book. The witness clearly testified this was a log book that was maintained by Roche's Analytical Department. He is involved in requesting analyses -- and so are the other medicinal chemists at Roche -- requesting analyses by the Analytical Department.

He is fully aware, as he testified, his log book entry notebook exists, and he was in charge of the very project relating to the prodrug project development for valganciclovir hydrochloride. He directed this very research that is designated in this log book entry, notebook entry 18951-142-60, which appears in the X-ray powder diffraction --

THE COURT: The problem is, Mr. Pezzano,

assume for the moment that he can identify what was kept by this department. He has gone beyond that, to testify what he believes is an inaccuracy. He distinguished 294 versus 194. I can't accept that testimony from him. This document may come in as something that was maintained, but it comes in whatever it is, without him giving substance to whether that was an error or not. I don't know that Mr. Olson objects on that ground without testifying about what that 294 versus that 194 number would mean.

MR. PEZZANO: This witness has been involved, and exhibits that were marked in this very action. For example, DX-594 is one where the very valgan-ciclovir hydrochloride entry 79074-194 is identified on that document. Dr. Maag was involved. He authored that very document. So he is fully familiar with the designation 79070-194 --

THE COURT: What he says is -- this was his testimony when you asked him about that:

> "It is not absolutely correct in that the first five digits, 79070, designate the compound which is valganciclovir. However, the 294 would be used for acidic acid salt, whereas for the hydrochloride that was

supposed to be used as 194."

Then he goes on to say:

"We had a complex numbering system."

But he doesn't verify what they used. He can't tell us what they actually did in there. No, I can only accept this document as it appears. He is not the witness to be explaining if an error was done in transcription here or what was actually done on that day. I have the document for what it is. It says what it says, and we can draw inferences from it the same way he perhaps has, but he can't tell us definitively.

Your exhibit is admitted in the manner which it is, but the testimony is limited on that issue.

(Plaintiff's Exhibit No. 255 B was received in evidence.)

THE COURT: Let's go to 255 C.

MR. PEZZANO: They are the very laboratory notebook pages, and the witness testified he directed this very work on these laboratory notebook pages.

THE COURT: Did he ever see these laboratory notebook pages prior to this case?

Mr. Maag, did you see these laboratory notebook pages at any time when the work was being

done?

THE WITNESS: I do not recall the specific instances. I worked very closely with Paul Fatheree. I visited his lab. I reviewed the results, and I do not recall at what point I saw these notebook pages the first time.

MR. PEZZANO: It's about 15 years ago. Dr. Maag was in charge of the project, and he did, as he testified, clearly direct the very work that occurs on these pages; and, as he's indicated, he was familiar with the results and communicated with his co-vendors regarding those results.

THE COURT: What did he testify as to these pages in C?

MR. PEZZANO: He testified that he directed this work to be undertaken by his co-vendors and that they reported this work to him.

THE COURT: Now, Mr. Olson, your objection to C is what? I know you said you don't have the whole notebook. But with regard to these specific pages, what is your objection?

MR. OLSON: And, of course, it is not his lab book.

THE COURT: I understand.

MR. OLSON: An additional comment here, your

Honor, and it goes to not seeing the other pages is that the reason there is interest in these pages of this lab book, is that it bears this identification number, the dash 60, which they then try to apply to these other documents. The point here, your Honor, there may well be other pages from his notebook that we don't have with an acetate experiment perhaps that relates to this, but they are saying this relates to this, their hydrochloride experiment relates to what on their face are acetic acid experiments.

THE COURT: Let me understand how these notebook pages were produced and why only these were available on not the entire notebook.

MR. PEZZANO: This was the subject of intensive discovery in the case. We responded in detail in interrogatories 4 and 5 as to why this notebook is missing. We had a Rule 30(b)(6) deposition of Roche's designee Brian Buckwalter. He stated the entire notebook is missing, and the library has -- and this very document PTX-182, this is a Roche library record, that indicates the notebook which was stored in the library is missing.

THE COURT: How are these pages available?

MR. PEZZANO: These pages were available because there were invention disclosures that were

submitted to the attorneys as to what the invention of valganciclovir hydrochloride was, and, therefore, they were separate and apart from the notebook. That's why these pages exist, because they were separately documented and provided to the attorneys in connection with the prosecution of the patent application leading to the '953 patent, and, therefore, that's why they existed separately from the entire notebook in Roche's files. The entire notebook, however, to this date is missing, based on all the information I previously told you.

THE COURT: Where is Mr. Fatheree or Dr. Fatheree?

MR. PEZZANO: Mr. Fatheree is located in California. He is no longer employed by Roche. They did take Dr. Fatheree's deposition.

THE COURT: Was he questioned about these pages?

MR. PEZZANO: Yes.

THE COURT: What did he say?

MR. PEZZANO: He testified these pages were his work that led to the invention of the '953 patent.

THE COURT: Okay. I think what I'm hearing, Mr. Olson, more is I don't really think I have an issue of authentication, given all of that. I can

admit them, but I understand your argument will be as to the weight to be given to them because the other pages are missing.

In that limited context, I'll admit them, and you can make whatever arguments you want, whether they demonstrate all the work that was done or whether this is something else.

(Plaintiff's Exhibit No. 255 C was received in evidence.)

THE COURT: Mr. Olson.

MR. OLSON: Just to remind your Honor, this is, basically, we are treating this as our direct.

THE COURT: I understand. We had this discussion last week.

DIRECT EXAMINATION

BY MR. OLSON:

Q. Good morning.

A. Good morning.

Q. Dr. Maag, just to try and make this go as easily as possible, you have been handed a binder, and that binder contains, at the front, your two depositions that were taken in this case, which we may or may not refer to, but they are there.

And then following that, there are a series of

exhibits, and they are arranged by DX numbers first. So I'll call out DX chronologically; and after all the DX numbers, there are PTX numbers, which are at the back, and those are Roche's numbers. Okay?

A. Okay.

Q. Now, I have a question for you with respect to a different scan than you were asked about in your direct. It's a scan that's in evidence, and it is in the back of your binder, and it's PTX-281 A.

This is another scan different than the one you looked at this morning, 255 A. Correct?

A. Correct.

Q. But similar format, similar style. I don't mean the scan itself, the information?

A. Yes.

Q. Now, will you agree with me, like the 255 A scan, it bears an ID number on the scan?

A. Yes.

Q. And, specifically, that ID number is 79070 Lot 108, and then slash ETOH, which, can we agree, Doctor, that would stand for the solvent ethanol?

A. Yes.

Q. If we look at one other scan, 282 A, which is also in evidence, that's another XRD scan, and it also bears an ID number on it, and that ID number is 79070

Lot 108/ethanol/two-hour ambient. Again, the ETOH would refer to ethanol?

A. Yes.

Q. And can we agree the two-hour ambient would be subjecting the sample to two hours of ambient conditions?

A. Right.

Q. Now, if we look at DX-104, this is a Roche preformulation book that is already in evidence.

Do you recognize it?

A. Yes.

Q. And it bears your name on the front of the document. Correct?

A. Correct. I'm on the distribution list.

Q. So you would have received a copy of this at the time?

A. Yes.

Q. And the time here is about -- it's dated March 22, 1996?

A. Yes.

Q. Then if we go to page 18 of DX-104 excipient, do you see that there is a scheme 1 with various forms indicated on that page with various letters, and the letters are identified below the scheme.

Do you see that?

A. Yes.
Q. And if we look at E, "E" is recrystallization from ethanol. Do you agree I read that correctly?
A. Yes.
Q. So this document indicates that if you recrystallize form X with ethanol, you obtain form B.
I'm just asking you whether this document indicates that on this page?
A. This scheme indicates that.
Q. And the arrow here is shown as a one-way arrow, not as a reversible arrow. Would you agree with that?
A. Yes.
Q. Now, I would like to move to a different topic; and, really, for the rest of the time here this morning, I would like to discuss with you your declaration that you submitted to the patent office in connection with the '953 patent. All right?
A. Yes.
Q. So let's look at that declaration. It's DX-180.
Do you recognize this as the first page of DX-180, your declaration?
A. Yes.
Q. Let's just turn to the last page 8 to see that it bears a signature. And will you confirm that's your signature?

A. Yes.
Q. And it bears a date of April 6th, 1999, which would be the date that you executed this declaration?
A. Correct.
Q. Now, let's turn to page 7 of DX-180, which is the previous page. And there is a conclusion section.
Are you with me?
A. Yes.
Q. And if we look at the first sentence of that conclusion. That's a fairly long sentence. It's on the screen. It's blown up.
I would like to focus you on a particular clause of that sentence, a particular aspect of the sentence, and it is highlighted, and let me read that. In the conclusion you make the statement:
"And the inability of others to prepare crystalline ganciclovir mono-L-valinate acetate."
Did I read that correctly?
A. Yes.
Q. That was one of the conclusions that you drew in your declaration. Is that fair?
A. Yeah. This is probably the first time I realized that there is a clear error in this statement, in that the second half of the sentence

should read:

"And the ability of others to prepare crystalline ganciclovir."

THE COURT: Why don't you go back and just answer the question Mr. Olson asked. He asked you: Was that one of the conclusions that you drew in your declaration?

THE WITNESS: Yes.

THE COURT: He answered it. He said, "Yes."

BY MR. OLSON:

Q. I'm directing my questions right now, Dr. Maag, to that particular statement, the inability of others to prepare the mono acetate.

Are you with me?

A. Yes.

Q. Now, you never personally prepared the mono acetate. Correct?

A. Personally, no.

Q. And at the time of this declaration, you were not personally aware of anyone who had tried to prepare the crystalline ganciclovir mono-L-valinate acetate?

A. The mono-L-valinate acetate was prepared in the fall of 1993, and I would need to refer to the notebook pages of Haiyingcai to ascertain what efforts

were made to crystallize his material.
Q. If I understand the point you are trying to make, you recall that someone prepared the mono acetate, I believe you said, in '93?
A. Right.
Q. But you don't know whether that was crystalline?
A. At the time I prepared this statement, I must have had additional evidence, which at the moment I don't recall.
Q. Well, let me ask it this way. I'm trying to get to the basis of -- first of all, are you now disagreeing with the statement in the declaration?
A. No.
Q. You are not trying to change the statement?
A. No.
Q. And the statement is the inability of others to prepare the mono acetate; right? That's the statement we are talking about?
A. Right.
Q. You are not trying to change that?
A. No.
Q. Now, I want to ask you about the basis that you made that statement in your declaration in 1999. This statement regarding the inability of others to prepare the monovalinate acetate was purely based upon the

fact that you were given this statement by your counsel at the time. Correct?

A. The declaration was prepared with counsel, and I included all the information which was available at that time to me.

Q. I appreciate that.

Answer my question the best you can. Maybe you did. My question is:

This particular statement -- I'm not talking about the declaration in its entirety, just this particular one.

I'm asking you if that statement in your declaration was based upon a statement that you had been given by your counsel. Yes or no?

A. Certainly this was written with the -- with counsel. However, at this very moment I do not recall what evidence I had at that point.

Q. Okay. Let me see if I can help refresh your recollection. I know your deposition was awhile back.

Let me show you what you said in your deposition. This would be page 175. It is your first deposition, page 175, and the line numbers would be 7 to 24.

Do you have the page now?

A. Yes.

Q. And the discussion here is talking about a summary of the inability of others to prepare the mono acetate, and you say yes."

And then there was a question:

"Did you review this summary?"

And you say:

"Well, the summary is what you have in the documentation.

So the question was:

"Just this sentence?"

Referring to the sentence we are talking about in the declaration.

And you say:

"To the best of my recollection.

"QUESTION: So you were only forwarded one sentence regarding the inability of others to prepare ganciclovir mono-L-valinate acetate. Is that correct?"

Objection.

"ANSWER: I don't have any recollection of any other information."

Other than being provided with this statement from counsel.

Is that a fair reading of your deposition we just looked at?

MR. PEZZANO: I object as mischaracterizing the testimony.

THE COURT: You have to go to the page before. This particular section doesn't say "counsel," but if you go to the page before it, I think it does. Let him go back and look at that.

MR. OLSON: I know what you are saying. Could we look at the page before, and could we look at the page after and tie it down.

THE COURT: I looked at the page before and there is a reference to "counsel."

MR. OLSON: Yes, there is, and that has to do with --

THE COURT: I guess the other was the bis.

MR. OLSON: Yes. Page 176, line 18, through page 177, line 14. So if we could see that.

THE COURT: All right.

BY MR. OLSON:

Q. So in line 18 it's:

"QUESTION: Well, I'm referring to this particular situation regarding the statements made here in your conclu-sion regarding the inability of others

to prepare" -- and it's referring to the bis and the mono. Both statements are in the question.

You say:

"ANSWER: I trusted the information I was given.

"QUESTION: Did you tell the patent office that you were given this information?

"ANSWER: I had no direct communi-cations with the patent office ever.

"QUESTION: Did you tell the attorney that you were just given this information?

"ANSWER: I indicated a few minutes ago that I received this information from counsel, so I don't understand your question.

"QUESTION: Okay. So is it correct to say that you received this information about the work of others from counsel?

"ANSWER: Yes."

Now, that we have looked at these two pages, does that help refresh your recollection that the basis for the statement in your declaration about the

inability of others to make the mono acetate was based upon a statement that you got from counsel?

MR. PEZZANO: Again, I'm going to say mischaracterizing the testimony there. I would refer to the last question and answer. It refers to information about the work of others from counsel.

THE COURT: I read all three or four pages now. It is clear what it is referring to.

Can you answer the question, Dr. Maag?

THE WITNESS: Can you repeat the question?

BY MR. OLSON:

Q. Now that we have gone through the deposition, before we went through the deposition, you didn't recall. You couldn't answer my question because you didn't recall. Now we went through the deposition pages.

Now I'm asking if it refreshes your recollection as to -- and here is my question -- whether the basis for your statement about the inability of others to make the mono acetate was based upon a statement you received from counsel?

A. Yes.

Q. All right.

Let's move on. Page 2 of DX-180. We are in your declaration still. We are just moving toward the

start of it.

Now, there is a section of page 2 entitled "Preparation of." It's the lower half of the page 2. Are you with me?

A. Yes.

Q. And it is also on the screen. It talks about the "Preparation of ganciclovir bis L-valinate acetate generally following example 5 of the Beauchamp patent on a reduced scale." Did I read that correctly?

A. Yes.

Q. Just for ease of reference, I'm going to call this the "first preparation." We are going to go through your declaration and see if there are other preparations you made.

Is it okay with you if I refer to this as the "first preparation"?

A. Yes.

Q. It says, "Generally following example 5." You will agree then you made modifications to the Beauchamp procedure?

A. Yes.

Q. And one of the modifications you made as an compilation was the reaction time that you used in preparation 1?

A. Yes. I also made changes in terms of the

reagents used in this experiment because Beauchamp prepares the protected L-valine in situ.

Q. So you are referring to one of the modifications you made.

Now I want to ask you about a modification you made with respect to reaction time. All right?

A. Yes.

Q. Now, in the preparation No. 1, the first preparation, it states in that first paragraph, you say you stirred at room temperature for ten days. Correct?

A. Yes.

Q. And I'll represent to you -- I don't want to take the time to look this up. It is in the record. I'll represent to you in example 5 of the Beauchamp patent she uses a reaction time of 18 hours.

A. Right.

Q. Do you have any reason to doubt that's correct, that she used 18 hours?

A. Right.

Q. You used ten days?

A. Right.

Q. The reason you used ten days was because when you set the reaction up here that you did, you then went on vacation?

A. That's in my deposition, yes.
Q. And you stand by that testimony?
A. Yeah. Also in the subsequent experiment, I stayed much closer to the Beauchamp conditions and got the same result.
Q. Thank you for that clarification.
Now, let's move to page 3 of DX-180 and see what you ended up with with this first preparation. You ended up with "4.4 grams of material," which you characterized as a glass. True?
A. Yes.
Q. And you characterized that as a glass solely upon your own visual inspection of the sample?
A. Yes.
Q. Now, you agree you could have, if you wanted to, you could have sent the sample out to XRD, the analytical, to assess crystallinity. You could have?
A. Well, in this particular case, I would refer to the next sentence in that it clearly demonstrates that this material was not a pure material, and, therefore, I would not carry out more detailed analysis with impure materials.
Q. You were trying to get pure material here. In your view, if you didn't get pure material, then you wouldn't be interested in sending it out for further

analyses?
A. Correct.
Q. Including XRD analysis?
A. Yes.
Q. But based upon your visual inspection of the sample, will you agree with me you could not rule out that there were at least some small amounts of crystals present in the sample?
A. Well, I would stick to my previous testimony, and the next sentence, in that it is to me very unclear what this material exactly was.
Q. And you didn't send it out to find out what it was; did you?
A. I did carry out an analysis and determined this was a mixture of product.
Q. You did not send it for any crystallinity analysis, sir?
A. No.
Q. Correct?
A. No.
Q. And as to this first preparation, there were no follow-on crystallization attempts as we'll see later in other preparations. Is that true? You did no follow-on crystallizations here?
A. Not with this sample.

Q. That's all I'm asking.

Now, let's go to the second preparation, page 4. This has the title, "Further Preparation of Ganciclovir Bis L-valinate Acetate." Correct?

A. Correct.

Q. I'm going to refer to this as the "second preparation" just for ease.

Now, in this one you report getting 6.2 grams of ganciclovir bis L-valinate acetate as an amorphous solid. True?

A. Yes.

Q. And you determined that this sample was amorphous purely by your visual inspection?

A. Correct.

Q. Again, you did not send this out for an XRD analysis to assess crystallinity?

A. No.

Q. No, you did not?

A. I did not.

Q. Now, let's look at something that happened in addition later on this. And to do that, we have to go away from your declaration for a moment to DX-305.

Now, DX-305 is a fax cover letter from you?

A. Yes.

Q. To a Mr. Von Morze. And he was the patent

attorney or one of the patent attorneys you were working with in connection with your declaration?

A. Correct.

Q. This is dated February 28, 1997. Correct?

A. Correct.

Q. If you would just look at the remaining eight pages of DX-305 -- just page through them, these pages comprise your experimental work to be incorporated into your affidavit, which was then under consideration for submission to the patent office. Correct?

A. Yes.

Q. And so we saw that your declaration DX-180 was signed in April, April 6th, 1999?

A. Right.

Q. We are two years earlier, roughly, here?

A. Yes.

Q. So as early as 1997, Roche was considering submitting a sworn statement from you for submission to the patent office?

A. That's what I understand, yes.

Q. It didn't actually get filed until 1999?

A. Yes.

Q. Will you agree with me that pages 2, 3, and 4 of DX-305 are the first preparation that we just

discussed that's recited in your declaration DX-180?
A. Yes.
Q. Will you agree with me pages 5, 6, and 7 of DX-305 recite the second preparation we just discussed in your declaration 180?
A. Yes.
Q. Now, let's talk about page 8, the last pages, 8 and 9 of this Exhibit DX-305. It is entitled "Experiment 3." Do you see that?
A. Yes.
Q. And this experiment is a follow-on working with the material that you obtained in the second preparation?
A. Yes.
Q. If we look at what you ended up with in this experiment 3, at the bottom of page 8, you report that:

"The mother liquor was pipetted off, and the crystalline residue was dried giving 3 milligrams of crystalline material third crop."

Did I read that correctly?
A. Yes.
Q. Now, this Experiment 3 was not included in your declaration that went to the patent office as filed in

1999. Correct?

A. That is correct. It represents a failed experiment; and, basically, I ended up with material which I was unable to identify.

Q. Okay. You jumped way ahead of me, but that's fine.

Now, you will agree with me all of the experiments of DX-305 were presented in your declaration -- I think we just saw that -- except Experiment 3. Do you agree with that?

A. Yes.

Q. Now, you just gave me an answer to a question I hadn't asked yet. But why wasn't it included in your declaration? And you indicated that it was a fail experiment?

A. Yes.

Q. And you were unable to identify the three milligrams of crystalline material?

A. Correct.

Q. You characterized it as failed, and you did in your deposition, because you didn't get enough pure material?

A. Yeah, it's very clear. This experiment was done 1 1/2 years after I prepared the sample. The goal at that point was to prepare a reasonable quantity of

pure materials so we could carry out some testing. I went through the steps and ended up with three milligrams of something which to this day I cannot identify. So I basically stopped and did something else.

Q. So to this day you don't know what it was?

A. No.

Q. All right. And you didn't send it out for analysis for XRD or any other kind of crystallinity analysis to figure out what it was. Is that fair?

A. No. I did basically a chromatogram on my own, and that was -- and that was the level of characterization I carried out.

Q. In answer to my question, you didn't do any testing to assess crystallinity?

A. No.

Q. No, you did not?

A. I basically --

Q. Your answer was confusing. Maybe it was my question that was confusing. I want to make sure, no, you did not; that you are not disagreeing with me.

Did you send this out for any further crystallinity assessment?

A. No. Not beyond my own assessment.

Q. Doctor, in your declaration -- let's recall.

You state under oath in the declaration, you make the statement -- and we looked at it -- that it is not possible to make the bis-valinate acetate ester. But here, do you agree with me you are making three milligrams of crystalline material, and you are stating here on the witness stand that you have no idea what it was. And, yet, in your declaration, you are making the statement it's not possible to make this bis-valinate acetate ester.

Is that a fair assessment?

A. Well, I believe that the 3 milligrams is not valinate bis-acetate.

Q. Doctor, you don't know what it was. You just stated you don't know what it was. True?

A. True.

Q. Now, I just want to tie this DX-305 to your lab book very quickly. DX-181, if you could turn to. That is a portion of one of your lab books, DX-181. And if we look at page 3, will you agree with me that we see at the top a so-called purification experiment in I think it's April of 1994?

A. Yes.

Q. And this is the Experiment 3 that we were just looking at, the typed-up version that you did for your patent attorney in DX-305?

A. Yes.
Q. So this experiment occurred in about April, May 1994?
A. Correct.
Q. That's long before your declaration in 1999?
A. Yes.
Q. And on this page you report the results, and we have highlighted it on the screen. You report that you got crystalline residue, and below it you indicate about 3 milligrams?
A. Right.
Q. And the word "crystalline" is underlined; and, in fact, it appears to be the only word in the whole page that's underlined. Do you agree with me?
A. I don't know how the underline arrived. It's certainly not something I would do in a notebook.
Q. You would agree with me this is your book and it is underlined?
A. It is now underlined.
Q. Let's go on and talk about the third preparation. Let's go back to DX-180. That's your declaration. And the third preparation starts on page 5.

Are you with me?

A. Yes.

Q. The title there is on the screen. This is preparation of ganciclovir bis L-valinate acetate, generally following example 5 B of the Beauchamp patent at a larger scale. Right?

A. Yes.

Q. Now, if we look at DX-8, that's a large file wrapper history, but it is in your binder as becomes 8. Specifically, page 43 of 350. Are you with me?

A. No. I'm lost.

Q. It's DX-8 in your binder.

A. Okay.

Q. And if you would turn to page 43. Underneath the DX-8, you will see various numbers of 350, and this is 43 of 50 that I am on.

A. I got it.

Q. Do you recognize this? This would be a portion -- this is a page from the application that eventually became the '953 patent?

A. Okay.

Q. We are on page 43 of the exhibit, but I'll just note for the record it is page 29 of the application on the bottom there, and it's lines 9 through 18.

Could you read that paragraph to yourself, and let me know when you are finished.

(Pause.)

A. Okay.
Q. Do you agree with me this paragraph discloses numerous ways to crystallize the mono-valine ester?
A. Yes.
Q. Do you agree these disclosed ways are not special or uncommon procedures?
A. The procedure outlined here is not special. However, it is still surprising this diasteric mixture crystallizes.
Q. I'm just asking you whether these crystalli-zation procedures that are outlined here are special or uncommon. That's all I'm asking you right now.
A. They are common.
Q. And in your declaration you did not try each of these procedures recited in your application on any of the preparations. True?
A. I'm not quite following. In the declaration it refers to the crystallization of the bis-valine material.
Q. And I'm not trying to jump around on you. Let me try to be clear.

I'm asking you whether you applied each of these procedures in the preparations in your declaration.

A. I applied quite a number of conditions as

detailed in the declaration. I would segregate in terms of attempts, solvents such as alcohols, chlorinated solvents, tetrahydrofuran and aromatic solvents, and all these different conditions are actually detailed in my declaration.

Q. Are you sitting here telling me you tried all these procedures as outlined on this page in your preparations for crystallization attempts?

A. What I stated in my declaration I used different solvent systems, and I think they represent a detailed approach to mimic most of the conditions outlined here.

Q. But not all?

A. No.

Q. "No," not all? "No," you did not use them all?

A. That would be impossible.

Q. Okay. It's impossible.

Let's look at what recrystallization attempts you did make, sir. All right?

A. Yes.

Q. Let's look at those six attempts. Correct?

A. I don't recall the exact number.

Q. I'll refresh your recollection.

Let's look at DX-180. Let's go to page 6 because we want to talk about the recrystallization

efforts, page 5.

We are talking about the third preparation, and we see at the bottom of the page you tried various crystallization attempts, and they are outlined on page 6 and 7?

A. Yes.

Q. And there are six attempts?

A. Yes.

Q. Now, if we look at the first attempt on page 6 -- we have that on the screen, this relates to the first recrystallization attempt, and the result was that you obtained, quote, "the GBVA formed in oil."

A. Yes.

Q. Now, if we go to your notebook, that's DX-182, and let's see that work in your notebook, 182, page 7. Are you with me?

A. Yes.

Q. The bottom third of the page, there are some experiments on March 15 and March 16 of 1999. Do you see that?

A. Yes.

Q. And across the bottom of the page there is a Roman numeral I and a 2 and 3 and 4. Those relate to these various crystallization attempts?

A. Yes.

Q. If we want to look at the first one, it's the very left-hand part of the page, and it is underneath the title, "Crystallization Attempts." Do you see that?

A. Right.

Q. So we see the result of March 16, 1999 at the bottom was "oil" -- I can't read the word.

A. "Oiled out."

Q. And then you referred to page 46?

A. Correct.

Q. Which would be a reference to a further page from your notebook?

A. Yes.

Q. So let's turn to page 11 of DX-182, and we see that page from your notebook. Correct?

A. Yes.

Q. And where in -- now, we are on April 14 of 1999, and you referred to a continuation of sample 1, page 42?

A. Yes.

Q. So I guess you are roughly about a month later than the previous work we looked at?

A. Correct.

Q. And you say that -- and I'm quoting:

"This week it was noticed that some

crystals had formed in this flask."

Did I read that correctly?

A. Yes.

Q. And then on the 15th you referred to 38 milligrams of material?

A. Yes.

Q. And then your conclusion on this experiment is the last paragraph on that page, and we have it on the screen. We are on page 11 of DX-182.

Your conclusion that you state is:

"Data most compatible with a mixture of mono- and bis-valinate and 1 or less than 1 equivalent of acidic acid."

Did I read that correctly?

A. Yes.

Q. That was your conclusion as to what that material was at the time?

A. Yes. Based on the analysis which is listed above.

Q. And that analysis is NMR and MS?

A. Yes, as well as elemental analysis.

Q. So here you have a mixture -- in your own words, you've got a mixture of mono- and bis-valinate that was crystalline?

A. Yes.
Q. And you didn't submit it for any crystallinity analysis?
A. No.
Q. No, you did not?
A. I did not. It's not a pure sample.
Q. I understand this qualification you keep making. It's not pure, and you didn't do further analysis?
A. Right.
Q. Now, this continuation is about one week after -- so we are in April 15, 1999. Do you recall your declaration was April 6, 1999?
A. Correct.
Q. We are about one week after you signed your declaration?
A. Yes.
Q. Let's look quickly at DX-8 again. It's the application page 177.
Do you have that page?
A. Yes.
Q. Now, this is entitled "Response to Office Action." Did I read that correctly?
A. Yes.
Q. And at the top there is a signature by a Derek Freyberg. Do you recognize that name?

A. Yes.
Q. He was one of the patent attorneys you worked with in connection with your declaration?
A. Correct.
Q. And the response refers in that paragraph to:
"Please enter the following amendment and accompanying declarations of Charles Dvorak and" yourself "Hans Maag."
A. Correct.
Q. This is a reference to the DX-180 declaration that we have been looking at?
A. Yes.
Q. And you would agree this certificate of mailing at the top indicates that it was submitted to the patent office on June 7, 1999?
A. That's what it shows, yes, correct.
Q. And right after your name, there is a reference to "which are copies of those submitted but not entered in parent application number" and it gives the number, the '223 application.
Did I read that correctly?
A. Right.
Q. Now, we talked about the first crystallization. Let's talk about the second one. We are in the third

preparation. Let's go back to DX-180, page 6.

So we are in the second attempt, and we have that paragraph on the screen, one paragraph. Do you see it?

A. Yes.

Q. And in this second crystallization attempt you obtained what you refer to as an amorphous precipitate of GBVA formed"?

A. Correct.

Q. And you determined that it was amorphous purely visually?

A. I believe so, yeah. We'll need to go back. If I can check back with my notebook.

Q. That would be DX-182. I think you want to look at the seventh page. I think that's probably what you wanted to find, isn't it?

A. Yes.

Q. So you are checking now the second crystallization that's identified in your notebook DX-182 on page 7?

A. Right.

(Pause.)

Okay.

Q. You determined it visually?

A. The notes in my notebook is from my visual

inspection, yes.
Q. Now, let's look at the third recrystallization attempt.
THE COURT: When you finish this, we will break; and today we will take a .45 minute lunch hour. We won't take an hour.
MR. OLSON: I probably have 10 minutes left of cross.
Q. DX-180, page 6.
A. Okay.
Q. That's the third recrystallization attempt?
A. Okay.
Q. Let's look at -- we'll get it on the screen. It's on the screen now. Is this third attempt you say, "a few needles appeared." Right?
A. Yes.
Q. And, of course, the needles would be crystals?
A. Yes.
Q. And the result you say:
"The drying resulted in 3 milligrams of a mixture of crystalline and amorphous material."
Did I read that correctly?
A. Yes.
Q. And, then, if we go to your notebook DX-182,

that same page, that page 7 we are going to find your third recrystallization attempt. Right?

A. Yes.

Q. It indicates, "a few crystals/needles."

Do you see that?

A. Yes.

Q. And then if we turn two pages to page 9 of DX-182, we see the continuation of crystallization attempt No. 3. Correct?

A. Correct.

Q. And let's just look at the conclusion that you drew there at the very bottom.

Conclusion:

"Crystalline material is most likely bis-ester in a different pronated or neutral form."

Did I read that correctly?

A. Yes.

Q. And you agree you did not send this material for crystallinity analysis?

A. No. I indicated through my analysis that it was a mixture.

Q. But you didn't send it for crystallinity analysis. Correct?

A. No, I did not send it out.

Q. Just to kind of sum things up, Dr. Maag, and try to finish this up so I can say I'm holding my time limits here, we have now looked at three different experiments in which you obtained crystalline material. Do you agree with me?

Let me categorize them for you. The Experiment 3, which was the purification of the second preparation; the continuation of the first recrystal-lization of the third preparation, and the third recrystallization in the third preparation, in all three of those experiments you obtained crystalline material. True?

A. True.

Q. In two of those instances of obtaining crystalline material, that was not even reported to the patent office examiner.

Let me categorize those two: The Experiment 3, which was the purification of the second preparation, and the continuation of the first recrystallization were not reported to the examiner. True?

A. Yes.

Q. And you never sent any of those three crystalline samples out for crystallinity analysis. Correct?

A. That is correct. We used these very small amounts to see if it could induce progressive crystallization to actually see if the material would crystallize, but none of these were ever successful. So we concluded that whatever the material was, it could not be bis-valinate bis-acetate.

Q. Sir, you didn't send them out for crystallinity analysis to determine what those materials were; did you?

A. No, I did not.

Q. In fact, you even testified today as to several you didn't know what they were because you didn't send them out for analysis. Correct?

A. I did not send them out.

Q. And as to several other experiments we have looked at, you obtained solids and you characterized them as amorphous solids. We have seen that. Right?

We took the time to go through this, and we saw several times you characterized solids that you obtained as amorphous?

A. Yes.

Q. And you did that purely by visual inspection. Correct?

A. Correct.

Q. And you didn't send them out for crystallinity

analysis to determine if there was perhaps a small amount of crystalline material within that amorphous material. You didn't check that; did you?

A. No, I did not.

Q. Because you were looking to see if you could produce relatively pure ganciclovir bis-acetate in crystalline form. Right?

A. Yeah, that is really the objective, to prepare a pure material in crystalline form.

Q. You weren't looking to see if you could produce small amounts of crystalline material. That wasn't the object of these experiments. Correct? You were trying to get pure material, not worried about whether you had small amounts of crystalline material. Correct?

A. Well, as a chemist, I want to see if I could repeatedly crystallize a sample in order to get anything that's useful.

Q. I'm not talking about what you considered as useful. You were looking for pure crystalline material. You weren't interested if you might have had a small amount of crystalline material. Correct?

A. I was interested in small amounts as long as I could identify it as a pure material. That's what I was after.

Q. And in these situations you did not even send them out for crystallinity analysis to determine what you had. Correct?

A. I did not send them out.

Q. So in your declaration, sir, rather than saying -- you said in your declaration it's not possible, it's not possible to make the bis-acetate in crystalline form. That's what you said in your declaration. True? That's what you said.

What you really meant by that, sir, was that you were unsuccessful in obtaining the bis-acetate as a pure material in crystalline form. Correct?

A. Yes.

MR. OLSON: Thank you.

Your Honor, housekeeping. I'm moving into evidence DX-181, DX-182, DX-305, and that's it.

MR. PEZZANO: No objection. I just have one or two questions.

THE COURT: Let's do it so we can finish the witness. They will be admitted in evidence.

Thank you.

(Continued on the next page.)

(Defendants' Exhibits Nos. DX-181, DX-182, DX-305 were received in evidence.)

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REDIRECT EXAMINATION

BY MR. PEZZANO:

Q. Dr. Maag, I just want to direct you to your declaration, DX-180, at the sentence in paragraph 6 on pages 6 and 7 of your declaration.

You state:

"From these data I conclude that the crystalline material is a neutral or partial salt form of ganciclovir bis L-valinate and not GBVA which explains the formation of only a small amount of crystalline material and the lack of progressive crystallization."

What did you mean by not GBVA?

A. I referred to GBVA to ganciclovir bis-valinate bis-acetate.

Q. And did you conclude that the small amounts of material were not ganciclovir bis-valinate acetate?

A. I concluded from the behavior of this material and the analysis I did that this was not bis-valinate bis-acetate.

Q. And you reported that in your declaration filed to the patent office. Correct?

A. Correct.

MR. PEZZANO: I have no further questions.

THE COURT: Thank you, Dr. Maag. You are excused.

(Witness excused.)

THE COURT: We'll break for lunch.

THE CLERK: All rise.

(The luncheon recess is taken.)

(Continued on the next page.)

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A F T E R N O O N S E S S I O N

(In open court.)

THE CLERK: All rise.

THE COURT: Thank you. Everyone may be seated.

Mr. Pezzano, you may proceed.

MR. PEZZANO: Your Honor, on behalf of plaintiff Roche Palo Alto, LLC, our last witness will be Dr. Jan-Olav Henck on rebuttal.

THE COURT: I guess it has been awhile. So why don't we swear in Dr. Henck today.

JAN-OLAV HENCK, recalled as a witness on behalf of the plaintiff, having been first duly sworn, testified as follows:

DIRECT EXAMINATION

BY MR. PEZZANO:

Q. Dr. Henck, do you recall on your direct testimony you were questioned by the Court as to whether there is any published literature that reflects that all you need is one peak to identify a crystalline material and, in particular, in distinguishing between a crystalline material and an

amorphous material?
A. Yes.
Q. And you replied you were both aware of industry-wide recognized articles that do this and patents?
A. Yes.
Q. Did you bring with you any articles and patents here today?
A. Yes.
Q. I would like to direct your attention to your binder PTX-752.
A. Yes.
Q. Is the article entitled "Pharmaceuticals Development and Formulation," an article you co-authored with Joel Bernstein in a textbook entitled, "Industrial Applications of X-ray Diffraction," which was published in 2000?
A. Yes.
Q. Is this a peer-reviewed and industry-recognized article in the field of polymorphism and powder X-ray diffraction?
A. Yes.
Q. Turn to page 530 of this article.
What is described here in reference to the Court's inquiry?
A. On page 5130, if we go to the middle of this

page, there is a topic called "Qualitative Analysis." It refers to an example where the X-ray diffraction powder patterns are on the previous page 529. It refers to a drug formulation called Excedrin.

Excedrin contains three different drug substances: No. 1 being acetaminophen, aspirin, and caffeine. When we look at the X-ray diffraction powder given on page 529, the X-ray diffraction powder pattern at the top of the page shows the tablet formulation, and the subsequent powder patterns are the X-ray diffraction powder patterns of the pure components.

For the X-ray diffraction powder pattern of aspirin, we can identify the peak at 7.5 degrees, 3.5 degrees two theta. So when we look at this photograph, we can see for aspirin, we have a peak at 7.5 degrees two theta; and within the different components, this is the only component that shows the peak at 7.5 degrees two theta, and we can identify this peak also in the drug formulation. Only one peak is necessary. This is what is stated on page 5130.

When we look at another component in this drug formulation, acataminophen, when we look at the diffraction powder pattern of acetaminophen, we see we have a peak at approximately 18 degrees two theta, and

this can also be identified in the drug formulation because there is no peak for caffeine or aspirin at 18 degrees two theta.

Q. Let's turn now to a second article, PTX-768 in your binder.

Have you seen before this text entitled, "Amorphous Food and Pharmaceutical Systems" published by the Royal Society of Chemistry in 2002?

A. Yes.

Q. Is this peer-reviewed and industry-recognized journal in the field of polymorphism and powder X-ray diffraction?

A. Yes.

Q. In connection with this article, did you prepare a demonstrative relating to this article to assist you in responding to the Court's inquiry?

A. Yes.

Q. Let me show you PTX-764.

A. The example before showed if you have different crystalline materials, one peak can be used in order to identify crystalline materials.

The previous example was related to identifying different crystalline components by just using one single peak. In an X-ray diffraction powder pattern this example here shows how one peak can be

used in order to identify a crystalline material and an amorphous material.

So what we have here is a peak at 9 degrees two theta. We have to go back to the highlighted area here in the text. 9 degrees two theta and this peak was used to identify crystalline material, and later on also quantify the amount of crystalline material in a given sample. So just one peak. The peak at 9 degrees two theta was detected and used for this analysis.

Q. And if you look at each of the X-ray powder patterns, how would a person skilled in the art detect the crystalline material in this series of X-ray diffractograms?

A. This series of X-ray diffractograms, what's also called a waterfall plot, shows the increase of crystalline material by the intensity of the peak at 9 degrees two theta.

So the authors are stating in this article the lower amount is about 2 percent of crystalline material up to 60 percent of crystalline material.

Q. And in the text itself, is this information found on page 225?

A. Yes.

Q. Now, I would like to direct your attention to

PTX-716, another article in your binder?
A. Yes.
Q. Have you seen this article entitled, "Quantifying Low Amorphous or Crystalline Amounts of Alpha-lactose Monohydrate Using X-ray Powder Diffraction Near Infrared Spectroscopy and Differential Scanning Calorimetry" that was published in 2004? Correct?
A. Yes.
Q. Is this a peer-reviewed and industry-recognized journal in the field of polymorphism and powder X-ray diffraction?
A. Yes.
Q. If you turn to page 517 of this article, what is described here in reference to the Court's inquiry?
A. When we go to the middle of the first column, it starts:

> "Therefore, the evaluation of the crystalline content is done using the profile fitted area under the peak at 12.4 degrees two theta; whereas, the amorphous content is evaluated by calculating the ratio of the next intense peak of all peaks to the observed intensity over the whole

range."

Q. I would like to refer your attention to the next article, which is PTX-770 in your binder.

MR. ZIMMERMAN: Your Honor, at this point I have an objection to 770 through 774. 770 is not a one-peak reference by any stretch. The other ones were responsive to your inquiry. I didn't have an objection. That's not what this one goes to.

MR. PEZZANO: It is responsive to your inquiry. I will ask the witness questions. If your Honor feels it is not responsive to your inquiry, then it won't be admitted into evidence. If you feel it is, and we believe it is responsive.

MR. ZIMMERMAN: If the witness uses it in a one-peak fashion, then I don't have an objection.

THE COURT: So we will wait and hear.

BY MR. PEZZANO:

Q. Have you seen before this article entitled, "Some Physiochemical Properties of Glassy Indomethacin," and that was published in the Chemical Pharmaceutical Bulletin in 1986?

A. Yes.

Q. Is this a peer-reviewed and industry-recognized literature reference in the field of polymorphism and powder X-ray diffraction?

A. Yes.
Q. If you turn to pages 4319 to 21, including reference to figure 10, can you describe how this article relates to the Court's inquiry?
A. Yes. When we look at figure 10 in this paper, what we see is that the drug substance was stored at laboratory conditions and is going from an amorphous to a crystalline material over time.

Your Honor, you asked me how difficult it would be to identify crystalline material and amorphous material. When you look at the powder presence here, when they are progressing from amorphous material to crystalline material on the arbitrary units, what you will see is there are so many peaks in the X-ray diffraction powder pattern that you can use in order to identify a crystalline material that it really doesn't matter which peak you use when you compare amorphous to crystalline material overall.

Q. What were the conditions over which this article describes that the material here converted to crystalline material?
A. Let me go into the paper.

It says, on page 4320, in the middle of the page, it says --

MR. ZIMMERMAN: Your Honor, this is where I'm going to renew my objection. This reference does not go to one peak. Dr. Henck just testified you could look at many peaks. He's using this to discuss the solubility, and the solubility issue is not in his expert report. This exhibit was not in their expert report, and it is not on his exhibit list.

MR. PEZZANO: He didn't say "many peaks." He said you can use any peak of this material. As it is converting from amorphous to crystalline, you can take any peak in that analysis to identify a distinction between the crystalline material and the amorphous material.

Second of all, he didn't mention anything about the issue of solubility.

THE COURT: I don't need anything else. I don't know why we're going into more testimony. It's getting in through the back door. It's not necessary. I heard his testimony about any peak. That's enough.

MR. PEZZANO: Now, that's the last of the articles. We just have a few patents the witness has collected and he would like to testify about in response to your inquiry.

THE COURT: That wasn't my question. I asked for literature. That's what I asked him about.

MR. PEZZANO: Okay. We'll move on.

BY MR. PEZZANO:

Q. Dr. Henck, I would next like to direct your attention to the medical pill organizer study of Ranbaxy's tablets and Dr. Rogers' testimony regarding that study.

Were you present for Dr. Rogers' testimony?

A. Yes.

Q. Did Dr. Rogers have access to your peak data underlying your powder X-ray diffractograms resulting from your study?

A. Yes.

Q. Did Dr. Rogers critique the results of your peak data and powder X-ray diffractograms for that study?

A. No.

Q. I would like to show you PTX-698. It's in your binder. Feel free to reference those exhibits during the course of my questions.

Showing you Exhibit 698, which includes PTX-581 through PTX-585. These are your X-ray diffractograms in connection with your medical pill tray organizer study that was over a period of five weeks. Correct?

A. Yes.

Q. Is it fair to say Dr. Rogers did not critique

the underlying peak data for any of the -- if you turn to the next slide and the next one -- any of the 3.5 degrees two theta peaks that are in your X-ray diffractograms as part of this study?

A. I'm sorry. Can you repeat the question, please.

Q. Is it fair to say Dr. Rogers did not critique the underlying peak data for any of the 3.5 degrees two theta peaks shown in your X-ray powder diffractograms?

A. Yes.

Q. I would like to direct your attention to Dr. Rogers' testimony concerning the methodology you used for the medical pill tray organizer study.

Did you prepare a demonstrative to assist your testimony regarding your methodology for that study?

A. Yes.

Q. Let's turn to PTX-765.

A. Yes.

Q. Is this the demonstrative you prepared in connection with your medical pill tray organizer study?

A. Yes.

Q. Do you recall Dr. Rogers' assertion that the tablets in your medical pill tray organizer study were ground in a mortar and pestle increasing the surface

area of the tablets and exposure of the tablets to moisture in the atmosphere?

A. Yes.

Q. What is your response to that testimony?

A. The tablets were rendered into a powder so they were not ground. We used 10 tablets total for the times zero testing in order to show that the procedure that we have used does not induce crystalline material into the sample.

Moreover, we have eight more samples that were tested after 24 hours that did not show an appreciable amount of crystalline material. So, in total, we have 18 of 80 tablets that show the procedure we have used does not induce appreciable amounts of crystalline material in Ranbaxy's tablets.

Q. And your testimony about the tablets were rendered into a powder, was that information found in any laboratory notebook records that were part of your study?

A. Yes. When we look at PTX-718, my staff wrote into that notebook each tablet sample was rendered a powder by lightly crushing it in a mortar and pestle. Each tablet was rendered a powder by crushing it in a mortar and pestle, and we can look this up in the notebook, and it's described there.

Q. Are those notebook pages found in your underlying binder, Binder No. 4, the big binder which we provided for you?

A. Yes.

MR. PEZZANO: It's in Binder No. 4, the medical pill tray binder.

Q. Let's move on to the next point.

Do you recall Dr. Rogers' assertion that the opadry coating was ground into each tablet in your medical pill tray organizer study?

A. Yes.

Q. What is your response?

A. We are dealing with a tablet here and removing a compound. For example, the coating of the material that was rendered into a powder is a significant flaw in the preparation of the sample for an X-ray diffraction experiment because when you grind the coating, what you will see is that on the part of the coating that was exposed to the core of the tablet there is material sticking on this coating and removing the coating means that you not only remove the coating from the sample, but you also remove other components from the sample; and, therefore, removing a compound of the sample can have a significant impact on the quality of the analysis. And, therefore, we

don't remove the coating from the material that was rendered into a powder.

Q. Do any of the elements in the opadry coating have a crystalline peak at 3.5 degrees two theta?

A. Our times zero studies show that the coating does not contribute to a peak at 3.5 degrees two theta.

Q. Now, turning to the first bullet on that page, do you recall Dr. Rogers' assertion that no duplicate powder pattern runs were performed for each tablet in your medical pill tray organizer study?

A. We did much better. We tested two tablets for every week in the times zero study. We tested individual tablets. We did not test one tablet multiple times. So measuring multiple tablets gives you much more available information in a study like this compared to running multiple powder patterns on one sample.

Q. In total, how many tablets were tested in your study?

A. 80.

Q. And this study was undertaken on a five-week basis. Correct?

A. That's correct.

Q. Now, I would like to direct your attention to

whether you recall Dr. Rogers' assertion that there were no controls between rendering tablets into a powder and each X-ray powder diffraction analysis in your study. Do you recall that testimony?

A. Yes.

Q. What is your response?

A. The tablets were rendered into a powder for testing immediately after they were removed from the pill tray organizer. This procedure -- we have years of experience in optimizing this kind of a procedure because we know that this is a critical step in performing the analysis. So the people that are doing these kinds of analysis are well trained and know exactly what to do. This kind of procedure takes about five to ten minutes overall.

Q. And on your direct testimony you testified that you were not present at all times when the tablets were rendered into a powder for your medical pill tray organizer study. How do you know each tablet was rendered into a powder and prepared for X-ray powder diffraction analysis in the same manner according to your protocol?

A. We have a very well trained staff and also have standard operating procedures. We are a GP lab, and the people we have trained follow these procedures

very carefully and to the word. So it doesn't matter whether I will be present for a specific study for not. These people know what they are doing.

Q. Dr. Henck, do you recall Dr. Rogers' criticism that you used an arbitrary Y scale in your study?

A. Yes.

Q. What is your response?

A. We undertake the pill tray study to get a qualitative idea of the conversion of Ranbaxy's API from an amorphous material into a crystalline material. And in order to be able to compare many different powder patterns using an arbitrary scale and normalized X-ray diffraction powder patterns is a well accepted way. It is not unusual to use this for representation purposes.

Q. And getting back to your earlier testimony, I believe you mentioned you had times zero tablets or control tablets that were used in your medical pill tray organizer study. Did Dr. Rogers criticize at all the methodology you used for the times zero tablets in your study?

A. No.

Q. I would like to direct your attention to your gastric fluid study.

MR. PEZZANO: Why don't we show DX-803.8 point

27.

A. Yes.

Q. Were you present for Dr. Rogers' testimony concerning his analyses of your gastric fluid study peak data and powder X-ray diffraction analyses?

A. Yes.

Q. What does Dr. Rogers' analysis of your gastric fluid study raw data show in DX-803.8.27?

A. It shows a peak at 3.5 degrees two theta for the tablets that were exposed to a gastric fluid, a simulated gastric fluid after half minute, one minute, two minutes, four minutes, and eight minutes. The times zero study does not show a peak at 3.5 degrees two theta, which means here we do not have appreciably amounts of crystalline valganciclovir hydrochloride.

Q. And based on Dr. Rogers' own analysis of the peak data underlying your X-ray powder diffraction analyses, what does his analyses show in connection with your conclusions?

A. First of all, these are our data. So these have been measured in my laboratory. In whichever way you represent the data, whether you choose to use the raw data or you choose to use normalized X-ray diffraction powder patterns, there is always a peak at 3.5 degrees two theta.

Q. And you referred to "normalized data." What do you mean by "normalized data"?

A. Normalization is a standard process when diffraction powder patterns are compared within one study. We need to take into account that we do not have -- we do not compare the times zero tablet when we look at the X-ray diffraction powder pattern from a physical point of view exactly to a tolerability that was exposed for one minute up to eight minutes or, later on, 50 minutes.

What we see is that during the experiment we change the composition of the tablets, which means we partially dissolve the coating, for example, and partially the outer core of the tablet will start to dissolve, which means we have different types of samples. So we need to take this into account when we compare these different powder patterns to each other, and a way to do this is by normalization.

Q. By the way, have you seen any documents where Ranbaxy normalizes data?

A. Absolutely.

Q. We'll get to that later on.

Does the fact -- did you normalize the data in your study analysis?

A. Yes.

Q. Does the fact that you normalized the peak data and Dr. Rogers did not affect your opinions regarding the gastric fluid study?

A. No. When you look at Dr. Rogers' representation of my data and you compare it to my presentation of my data, we both have a peak at 3.5 degrees two theta for the material that was exposed to the simulated gastric fluid after half a minute. We have in both cases a peak at 3.5 degrees two theta for one minute, for two minutes, for four, as well as eight minutes.

Q. And leaving that comparison on the Power Point, comparing your XRD analyses of the gastric fluid study toin Dr. Rogers' XRD analyses of the same peak data, does Dr. Rogers' XRD analyses change your opinion about whether at least a majority of Ranbaxy's valganciclovir hydrochloride API converted to crystalline form?

A. No.

Q. Why not?

A. Because in both cases what we see is that over time we see an increase of crystalline material when we look at the powder X-ray diffraction patterns that were obtained during the conduction of this study. The peak at 3.5 degrees two theta appears in all the different tablets and it is growing over time. Each

tablet will behave individually. Each tablet was analyzed separately, and it was analyzed by using an X-ray diffraction method where the amount of material would have an impact on the intensity of an X-ray diffraction powder pattern, and, therefore, it doesn't change my opinion.

Q. Now, Dr. Henck, were you here for the testimony of Romi Singh, the head of Ranbaxy's valganciclovir hydrochloride tablet formulations group?

A. Yes.

Q. Did you hear her testimony regarding a purported entropy theory, that Ranbaxy's tablets may dissolve before they crystallize?

MR. ZIMMERMAN: At this point, I object. He has no opinion in his report comparing the dissolution time to his purported crystallization rate. When I asked him at his deposition and at this trial if he knew anything about the dissolution rate for this product, he said, no, he hadn't studied it. It's clearly outside of the scope of his expertise and expert report.

MR. PEZZANO: This is a new theory that arose during the course of the trial. The second is Dr. Henck did specifically address his theory. He did the tests. He tested Ranbaxy's tablets and showed

exactly the fact that they crystallized before they dissolved. His 15-minute tablet dissolved, but the crystallized at 30 seconds, one minute, two minutes, four minutes and eight minutes. He did the tests. So he is perfectly qualified to testify on this point.

MR. ZIMMERMAN: He hasn't done any dissolution studies. If he wants to talk about what he did in the graphs. He didn't do any comparison of dissolution rate to alleged crystallization rate. He doesn't know what the dissolution rate of amorphous or crystalline is; and for him to talk about dissolution and compare it to a rate of crystallization is found nowhere in his report.

THE COURT: Are you going to go into that area? Is that your intent?

MR. PEZZANO: My intent was to basically ask him what does he agree with Romi Singh's testimony --

THE COURT: Agree with what part?

MR. PEZZANO: That her view was that the pills would dissolve before they crystallized without undertaking any tests to show that, and he would simply say what the basis would be for his testimony in rebuttal to that testimony.

THE COURT: But that's not something he opined on.

MR. PEZZANO: Your Honor, we are not talking about the rate of dissolution. We are comparing the fact the tablet crystallizes before it dissolves, and that is clearly within the scope of Dr. Henck's study. He showed in his study at the 15-minute point the tablet dissolved; and in the 30-second to eight-minute point, he showed the tablet crystallized; and all he is going to testify about is the fact the tablets crystallize before they dissolved. And that is within the scope of his study. He is not going to talk about the rate of dissolution.

MR. ZIMMERMAN: It isn't in his report. The only thing in his report about dissolution is at 15 minutes, the tablet was gone. If he is going to do any comparison between the tablet crystallized before it dissolved, he didn't talk about dissolution. I asked him about the dissolution rate of the amorphous material and the crystalline material at his deposition. He didn't know the dissolution rates, he hadn't studied them, he hadn't compared them.

MR. PEZZANO: I'm going to rebut, I believe the position we have taken right now is satisfactory to have Dr. Henck testify, but I'm going to also point out in his expert report, he specifically points out Ranbaxy's bioequivalent and comparative dissolution

studies support these conclusions concerning the fact that Ranbaxy's tablets crystallize when in a person's stomach --

THE COURT: That's different than comparing them. I want to hear where he's got talking about the dissolution versus crystallization, and which occurs first.

MR. PEZZANO: That crystallization occurs before dissolving? The only thing I can point to is his test that showed at the 15-minute point the tablet dissolved --

THE COURT: I'm not going to have him give a general opinion. If he wants to point out where it showed in his test, point that out as opposed to giving an opinion.

MR. PEZZANO: One of the sentences in his report, he states:

"If Ranbaxy," -- this is talking about Ranbaxy's dissolution studies.

"If Ranbaxy's tablets contained amorphous material in the beginning of the studies, this material transformed rapidly into crystalline valganci-clovir hydrochloride, which is then dissolved during the studies described

in Ranbaxy's ANDA."

THE COURT: If you want to talk about what happened in the study, that's okay, as opposed to opining or saying the views of Ms. Singh he supports; and, as a general matter, this is what happens. Feel free to talk about factually what he observed.

MR. PEZZANO: I will do that.

BY MR. PEZZANO:

Q. Dr. Henck, in connection with your gastric fluid study, what did you observe in relation to that study concerning the crystallization of Ranbaxy's tablets and their subsequent dissolving?

MR. ZIMMERMAN: Objection; leading.

THE COURT: That was. You will have to rephrase it.

BY MR. PEZZANO:

Q. In connection with your gastric fluid study, what did you observe in connection with the timing of the crystallization of Ranbaxy's tablets?

A. The conditions in the human body with the elevated temperature at 37 degrees centigrade, and the simulated water-based gastric fluid, we have conditions here that promote crystallization, and this is given in many literature citations where people are discussing the behavior of amorphous material during

dissolution testing where it crystallizes and, therefore, within minutes --

THE COURT: He just asked you what did you observe, please.

THE WITNESS: In our studies we observed the material crystallizes before it dissolves.

BY MR. PEZZANO:

Q. Now, did you hear Dr. Rogers' testimony that exposure of Ranbaxy's tablets to ambient conditions for any length of time after removal of the tablets from the warm, moist gastric fluid conditions in the stomach is what caused Ranbaxy's tablets to crystallize in your gastric fluid study?

MR. ZIMMERMAN: Your Honor, when he says "stomach," I assume he means simulated stomach in the question, just so we have a clear record.

THE COURT: Obviously, that's what we are talking about. Right?

THE WITNESS: Can you repeat the question?

BY MR. PEZZANO:

Q. Did you hear Dr. Rogers' testimony that exposure of Ranbaxy's tablets to ambient conditions for any length of time after removal from the warm, moist gastric fluid conditions in a simulated stomach is what caused Ranbaxy's tablets to crystallize in your

gastric fluid study?
A. Yes.
Q. Do you agree with that analysis?
A. No.
Q. Why not?
A. We have shown with the pill tray organizer study if the material is exposed to ambient conditions, it takes a couple of hours to see the crystallization of valganciclovir hydrochloride.

So the ambient conditions do not contribute to a crystallization of valganciclovir hydrochloride in the time of the preparation of the samples which takes place within a couple of minutes.

Q. Now, I would like to direct your attention to Dr. Rogers' testimony concerning the methodology you used in your gastric fluid study. Did you prepare a demonstrative in connection with rebutting Dr. Rogers' testimony?
A. Yes, I did.
Q. Let's show PTX-766.

Is this the demonstrative that you prepared in connection with rebutting Dr. Rogers' testimony regarding the methodology you used in your gastric fluid study?
A. Yes.

Q. Do you recall Dr. Rogers' assertion that your tablet samples removed from the simulated gastric fluid are exposed to moisture under ambient conditions prior to XRD analysis?

A. Yes.

Q. What is your response?

A. My response is what I stated previously. The crystallization caused by exposure to ambient conditions is significantly lower, by an order of magnitudes, than compared to the exposure of the warm and moist conditions that we have in the stomach. And so it takes between 24 and 48 hours to see crystallization after exposure of Ranbaxy's tablets to ambient conditions; and within the gastric fluid studies, it takes only a few seconds to see this type of crystallization. This is consistent with reports in the scientific literature we got in those types of studies.

Q. Do you recall Dr. Rogers' assertions regarding the length of time between removing the tablets from the simulated gastric fluid and each X-ray powder analysis including he referenced a 22 minute gap in preparing the 30-second tablet sample compared to 10- to 12-minute gaps for the other samples?

A. Yes.

Q. What is your response?

A. The sample preparation for this testing takes about 15 minutes plus or minus three minutes, and it is related to cleaning the sample preparation area, setting up a clean transmission sandwich holder for this expert in a metal ring, and a polymer film is used to prepare the sample, and then transferring the sample to the holder, and putting it into the diffractogram meter logging onto the instrument computer software, and loading the sample and running the scan program.

In our system, the operator of the instrument has the freedom to put in the LIMS comment before he or she starts the experiment, or you can do it afterwards. So it may appear a time difference where, in reality, the preparation time is consistent, a very short time range.

Q. On your direct testimony, you testified you were not present at all times when rendering the tablets into a powder and taking the XRD analyses were undertaken. How do you know each tablet was rendered into a powder in the same manner, according to your protocol?

A. We do those kinds of studies, those kinds of tests very often. We have very highly specialized

personnel that work on these kinds of tests. They work on the GMP and T, so they are highly trained and follow these kinds of procedures very carefully. So I don't need to be present at any moment in time to be sure they are following the protocol.

Q. You mentioned "GMP." What is that?

A. That stands for "good manufacturing practice." So we, as a company, as a lab, we perform tests on the GMP. We have been audited by the FDA numerous times. The last three audits in 2003, 2005, and 2007, did not yield to a single 483. So we have been approved by the FDA for our tests.

Q. You mentioned about a 15-minute timeframe for the analyses for the Simulated Gastric Fluid Study, the rendering into a powder and the testing in the XRD. Is that timeframe longer or shorter than the timeframe for rendering to a powder and X-ray diffraction analysis for the medical pill tray organizer study?

A. The preparation for the gastric fluid studies takes a little longer compared to the ones for the pill tray organizer because it is a different experimental setup.

Q. What do you mean it's a different setup?

A. The instrument that was used for the pill tray

organizer is the Shimadzu -- this is the name of the company that produces this kind of instrument, where the powder pattern is recorded in reflection mode, whereas for the gastric fluid studies we used the panalytical instrument, where the X-ray diffraction powder patterns are recorded in transmission. So it's a different experimental setup.

Q. Now, do you recall Dr. Rogers' assertion that rendering tablet samples into a powder in your study introduced more moisture into the samples?

A. Yes.

Q. What is your response?

A. The tablets were drip-dried and lightly ground to a fine powder with a mortar and pestle to collect the X-ray diffraction powder pattern afterwards, and the procedure is outlined in one of the binders that are describing the Simulated Gastric Fluid Study. So this would be in binder 3, I guess.

The times zero tablets were also rendered into a powder under the same conditions. So the moisture in the room, the room temperature does not contribute to a crystallization of valganciclovir hydrochloride.

Q. You mentioned the procedure is set forth in your book Binder No. 3 on the Simulated Gastric Fluid Study. What were you referring to specifically?

A. To the procedure that describes how the samples were prepared.
Q. The laboratory notebooks?
A. Yes, the laboratory notebooks.
Q. On another point, and the last point: Do you recall Dr. Rogers' assertion that the eight-minute tablet X-ray powder analysis had been independently scaled compared to the other tablet X-ray powder analysis?
A. Yes.
Q. What is your response?
A. All the powder patterns in this representation that I'd chosen were normalized. And so the eight-minute test -- the eight-minute X-ray diffraction powder pattern was normalized in a way like all the other powder patterns in this study.
Q. I would like to show DX-803.8.23.
Were you present for Dr. Rogers' testimony concerning his analyses of your crystalline seed study peak data and X-ray powder patterns?
A. Yes.
Q. And what does Dr. Rogers' analyses show in DX-803.8.23 of your crystalline seed study raw data show?
A. It shows with increasing amount of crystalline

material, we see a peak in the diffraction powder patterns of the spiked sample, but we also have a peak at 3.5 degrees two theta in the tablet samples.

Q. And based on your opinions concerning the crystalline seed study, does Dr. Rogers' analyses change those opinions?

A. No.

Q. Why not?

A. Because in whichever way you look at the data, whether you look at the raw data, look at the representation of the normalized X-ray diffraction powder patterns, what you see is a peak at 3.5 degrees two theta.

Q. I would like to show you Defendant's Exhibit 603, which is in your binder.

A. Yes.

Q. Pages 52 to 69 in that exhibit.

A. Yes.

Q. Are these the texts TXT raw data peak files of your crystalline seed studies?

A. Yes.

Q. How do you know that?

A. Because the file name, and I recognize the file name and I recognize this text file as being part of the study.

Q. And there were different file names on top of the various pages of this exhibit. Do they match up with the file names for your crystalline seed study?
A. Yes.
Q. Who downloaded and printed these TXT text raw data files?
A. My staff at SSCI.
Q. Have you reviewed these TXT text files for accuracy to assure that they match up with the electronic raw peak data generated for your crystalline seed study?
A. Yes.
Q. Did you use this raw data in your crystalline seed study?
A. Sure.
Q. And is this raw peak data the same data that Dr. Rogers used in his analysis of your crystalline seed study?
A. Yes.
Q. Now, were you present when Dr. Rogers criticized your visual evaluation of the XRD patterns as the basis for your conclusion that Ranbaxy's tablets 1 and 2 in your study included a crystalline seed?
A. Yes.
Q. Do you agree with Dr. Rogers' assessment?

A. No.
Q. Why not?
A. Because visual inspection is used --
MR. ZIMMERMAN: Your Honor, if I can have an objection. They are going to bring up a demonstrative that is going to refer to an FDA document that was not in Dr. Henck's report, not cited in his expert report, not produced during the course of discovery in this case, and not on the exhibit list, and they are going to purport to have him testify about it.
MR. PEZZANO: We haven't gotten there yet. But I will point out that this exhibit, the FDA guidance document, is publicly available information. It is referred to because it is in rebuttal to Dr. Rogers' testimony about the visual critique of Dr. Henck's analysis, and the FDA itself on its website advises a visual analysis of tablets is permissible. So that's the rebuttal, and this witness knows that based on his analysis of the FDA's website.
MR. ZIMMERMAN: It is not an analysis that was conducted anytime prior to him testifying he said today. It wasn't in the expert report. The FDA guidance wasn't on the exhibit list, and Mr. Pezzano isn't saying that. He is saying it's publicly available, and the witness is allowed to talk about

it.

THE COURT: I'll find out if he actually reviewed that FDA guidance, like we did with the witness this morning.

BY MR. PEZZANO:

Q. Do you agree with Dr. Rogers' assessment that visual analyses and opinions are improper in connection with the crystalline seed study?

A. No.

Q. Why don't you agree with that?

A. Because visual inspection is a method that can be used in order to identify materials, small amounts of materials in any given material; and the FDA has published several different guidelines for the pharmaceutical industry to validate analytical methods. And the document I'm referring to, Q2B "Validation of Analytical Procedures Methodology," and under topic 6 of this document --

MR. ZIMMERMAN: I'm going to renew the objection at this time, your Honor. The witness hasn't established he knew about this document before --

THE COURT: That's the question we are going to get now.

MR. ZIMMERMAN: And he never cited it in

response at his deposition when I asked him specifically about visual inspection. So if he knew about it at this time of his deposition, he should have talked about it. I asked him repeatedly about visual inspection, and not once during that deposition did he use the words "FDA guidance" anywhere.

MR. PEZZANO: Your Honor, I'll ask him the question: When did you become aware of the FDA guidance? And my response is --

THE COURT: I want to hear what he says.

BY MR. PEZZANO:

Q. When did you become aware of the FDA guidance information?

A. I was aware of the FDA guidance since approximately the year 2000-2001, because when I worked in the pharmaceutical industry, we had to work with these guidances.

THE COURT: This specific one about visual inspection, how are you familiar with it, and when did you become familiar with it?

THE WITNESS: I know the guidance Q2B where this visual inspection has been published since approximately the year 2000-2001.

THE COURT: Okay. You knew of it or you were aware of what its contents were?

THE WITNESS: I knew of it, and I studied the contents.

MR. ZIMMERMAN: Then that begs the question why it wasn't in his report when he talked about visual inspection, and why it wasn't discussed during the deposition when visual inspection was raised, and why it wasn't put on the exhibit list in this case. If he knew about it, there is no excuse for it not being in his Rule 26 disclosures.

MR. PEZZANO: My response is, he listened. He's using knowledge that he has. He's listened to the testimony of Dr. Rogers, Ranbaxy's expert, and he is simply rebutting that testimony. That's the only information I have at this time.

I asked him the question: When did you become aware of it? This is information that's knowledge in his mind. So he is simply rebutting testimony that was made in this trial. And I'm not really sure about the specific questions that were asked, why those questions didn't trigger the FDA guidelines. I don't have that information in front of me to respond to it at this point. I don't know the answer to that. That's the best answer I can give you.

THE COURT: Well, let me ask you this question, Dr. Henck:

After listening to Dr. Rogers testify, when did it come to your mind and how did it come to you that you would cite to this guidance?

THE WITNESS: Dealing with this study, the graphs I showed, the representation I showed, was a representation for a person skilled in the art. The limit of detection discussion that arose by Ranbaxy, from my point of view, this is a question that I think you wouldn't ask in this context necessarily because what you would do from an analytical point of view and what the FDA states in the guidelines, to look at the analytical results and see whether you can establish the limit of detection by visual inspection. I'm doing this all the time. I don't think about it anymore. This is what I'm used to.

THE COURT: Go ahead, Mr. Pezzano.

BY MR. PEZZANO:

Q. Who brought this to your attention, if anybody?

A. No one. I thought about this, and I said: Wait a minute. When I heard this testimony, Ranbaxy is working on the GP. They know this document. This is something that's natural in this industry.

THE COURT: Go ahead.

Q. Let me direct your attention to PTX-763 in your binder.

What is this document?

A. This is the document I'm referring to all the time, Q2B, "Validation of Analytical Procedures Methodology." This is available information. If you go on the web and go to the FDA website looking for guidance in the industry, you will find this document.

Q. Where does it find the information that you testified about, about visual evaluation?

A. This is under Roman numeral VII on page 7 of this document.

And it says on "Detection Limit," and it says, "Based on visual inspection."

"Visual evaluation may be used for noninstrumental methods, but may also be used with instrument methods."

The second topic is "Based on signal to noise."

Q. Now, I'm going to turn my attention to Defendant's Exhibit 551. If you can turn in your binder to that exhibit, and we will show it on the screen.

A. Yes.

Q. Have you seen this document before?

A. Yes.

Q. What is shown here?

A. This is a valganciclovir placebo tablet produced by Ranbaxy.

Q. Does Ranbaxy detect any peak in its placebo for magnesium stearate at 3.6 degrees two theta?

A. No.

Q. How about in the attached peak list? The second page of this exhibit in your binder.

A. No.

Q. By the way, in this attached peak list, did Ranbaxy normalize its peak data?

A. Yes.

Q. How do you know that?

A. When you look at the relative intensity scale at the right side of this Table 7, these are normalized intensity data; and, as I said, this is a standard procedure because what people skilled in the art do, they compare diffraction powder patterns from different sources. So it makes more sense to compare them on a relative intensity scale than on an absolute scale.

Q. Now, I would like to turn your attention to DX-552.

A. Yes.

Q. Have you seen this document before?

A. Yes.

Q. What is shown here?
A. This is a valganciclovir hydrochloride tablet from Ranbaxy that was exposed to 25 degrees centi-grade, 60 percent relative humidity for 35 days.
Q. Does Ranbaxy detect any peak in its tablets for magnesium stearate at 3.6 degrees two theta?
A. No.
Q. What about the attached peak list? Page 2 of this exhibit.
A. No.
Q. Did Ranbaxy normalize the data in its peak list on page 2 of this exhibit?
A. Yes, the relative intensities are given.
Can we go to the next exhibit. They are given on the right side in this column.
Q. I would like to direct your attention now to Plaintiff's Exhibit 699, which is your crystalline seed study diffraction analyses; and if you could turn to the last page of this exhibit.
I apologize. Go to the first page. That's your placebo analysis. Correct?
A. Yes.
Q. How have you compared your placebo analysis to the placebo analysis in Ranbaxy's Exhibits DX-551 and DX-552?

A. Yes.
Q. How does it compare?
A. We don't see a peak at 3.6 degrees two theta, and we don't have a peak at 5.4 degrees two theta. We also need to take into account this is the placebo mixture which means the concentration level of magnesium stearate in this tablet is more than 2 percent because the API is missing. So we cannot detect this on a 2 percent level. So it is not surprising if you look at an actual tablet that it is not analyzable. Or detectable.
Q. Let's turn to your actual analysis of Ranbaxy's tablets in your crystalline seed study PTX-7:45 and PTX-746:
A. Yes.
Q. Could the magnesium stearate in Ranbaxy's tablets have contributed to the peaks at 3.5 degrees two theta and 5.4 degrees two theta in your XRD analyses?
A. We have seen before for the placebo itself we do not see a peak at 3.5 or 3.6 degrees two theta. So I assume this is due to crystalline valganciclovir hydrochloride if we see a peak at 3.6 degrees two theta.
Q. How about at 5.4 degrees two theta?

A. At 5.4 degrees two theta there may be a small amount of magnesium stearate that is present and can be detected. What we have to take into account here is that the intensity of the peaks in magnesium stearate at 3.6 degrees two theta is significantly lower than the intensity of the peak at 5.4 degrees two theta.

Q. Now, I would like to direct your attention to -- did you hear Dr. Rogers' testimony concerning the methodology you used in your crystalline seed study?

A. Yes.

Q. Did you prepare a demonstrative rebutting Dr. Rogers' testimony and critique of the methodology you used in your crystalline seed study?

A. Yes.

Q. Let's show PTX-757.

Is that the demonstrative that you prepared to assist your rebuttal of Dr. Rogers' testimony concerning the methodology of your crystalline side study?

A. Yes.

Q. Do you recall Dr. Rogers' assertions that the X-ray patterns that you prepared were run over a period of 3.5 months, and the length of time between the rendering of the tablet into a powder and the XRD

analysis was unknown in your crystalline seed study?
A. Yes.
Q. What is your response?
A. As I stated earlier, we are operating under GMP. Our instruments are calibrated and maintained. So the quality of the powder pattern does not change as a function of time. So it doesn't matter whether there is a time difference of 3 1/2 months or not.

The placebo excipient mixture with crospovidone microcelac 100 and magnesium stearate was stored in a glass scintillation vial, and this can be found in the lab notebooks that are related to this study.

And, so, Ranbaxy themselves gave their tablets a shelf life of two years. So 3 1/2 months of the components that are making up the placebo, there will be no change from a physical as well as chemical point of view of these components.

Also, its spiked samples were kept in a kept vial and stored so that there will be no change over time. Then Ranbaxy's tablets were lightly crushed and then run on the XRD instrument.

Q. Let's turn to the next slide.

Do you recall Dr. Rogers' assertion that your crystalline seed study did not include a limit of detection analysis or a calibration curve?

A. Yes.
Q. What is your response?
A. We used the visual inspection to identify a peak at 3.5 degrees two theta, and we see an increase in analytical response of the mixtures for 0.1, 0.3, and 0.5 percent crystalline valganciclovir hydrochloride. This is in comparison with the tablets we can identify the small amount of valganciclovir hydrochloride in the tablets.

MR. PEZZANO: Your Honor, can we just take a real brief break? I have probably another 10 minutes.

THE COURT: What do you mean, Mr. Zimmerman? I'm hoping to not have more than 40 minutes.

THE COURT: At 4 o'clock I have to be out of here, not just out of the courtroom, but out of the courthouse. When I said 4:00, I really meant a little before. You guys are going to be running awfully close.

THE CLERK: All rise.

(Recess.)

(Continued on the next page.)

///

(In open court.)

THE CLERK: All rise.

THE COURT: Thank you. Everyone may be seated.

JAN-OLAV HENCK, resumed.

DIRECT EXAMINATION (continued)

BY MR. PEZZANO:

Q. Dr. Henck, do you recall Dr. Rogers' assertion that the samples in your crystalline seed study were not homogenous?

A. Yes.

Q. What is your response?

A. The samples for making up an analytical placebo were mixed geometrically, and this is the most homogenous sample you can get.

Q. And do you recall Dr. Rogers' assertion that no attempt was made to use the same manufacturer and specifications of excipients used in Ranbaxy's tablets to your crystalline seed study?

A. We used the same type of excipients from industry recognized suppliers. As far as I remember, Meggle is a company in Germany that makes microcelac 100. We use this supplier from the original supplier.

Magnesium stearate from Fischer, who is a recognized supplier in the industry, and crospovidone from Fluka, who is also a recognized supplier in the pharmaceutical and chemistry. And with all of these materials, we get Certificates of Analysis which shows this is the compound that we want and the chemical purity.

Q. Are those suppliers identified in the underlying laboratory notebook in your exhibit binder at PTX-577?

A. Yes.

Q. Did you hear Dr. Rogers' testimony regarding a partially ordered product that is not in crystalline form?

A. Yes.

Q. Do you agree with his testimony?

A. I respectfully disagree with Dr. Rogers. Materials can be crystalline or amorphous.

Q. And are you aware of any peer-reviewed and industry-recognized publications consistent with your testimony that there is only a crystalline form and an amorphous form?

A. Yes.

Q. I would like to show you PTX-772.

This is a tex by J.W. Mullin called "Crystallization," 4th Edition, 2001.

A. Yes.

Q. Have you seen this text before?
A. Yes.
Q. Is this an industry-recognized and peer-reviewed text in the field of polymorphism and powder diffraction?
A. Yes.
Q. If you turn to Chapter 1 in this text. It is in your binder, which is entitled, "The Crystalline State." What is discussed here?
A. This is the introductory chapter of this book. When we go into the middle of this page, we see it says:

> "Solids may be crystalline or amorphous, and the crystalline state difference from the amorphous state in the regular arrangement of the constituent molecules, atoms, or ions into some fixed and rigid pattern known as lattice."

J.W. Mullin in this book on crystallization is around for many, many years now. It is in its 4th edition, and some people consider it the bible for crystallization.
Q. Is there any mention here of a partially ordered form?

A. No.

MR. PEZZANO: I have no further questions. I'll read in my exhibits at the end.

CROSS-EXAMINATION

BY MR. ZIMMERMAN:

Q. Good afternoon, Dr. Henck.

A. Good afternoon.

Q. In the spiking study, the Simulated Gastric Fluid Study and the Pill Tray Study, you looked for a peak in the low angle region, namely a peak at 3.5 degrees two theta. Right?

A. That's correct.

Q. And you agree that there are solid materials with an intermediate order between that of a liquid and a crystal that exhibit X-ray diffraction patterns with one low angle peak. Correct?

A. If you are referring to, for example, liquid crystals, then my answer would be, yes, those materials would show a peak at low diffraction angles but may differ between what you refer to being a liquid crystal and the material we are looking at here, valganciclovir hydrochloride is a solid and liquid crystals --

Q. Dr. Henck, we have limited time. If you can

answer my questions directly.

I was talking about a solid. You agree there are solid materials --

MR. PEZZANO: I object. The witness was responding to that question. He was in the middle of an answer. I know we have a time constraint. The witness was providing an answer.

THE COURT: I think he was giving what his understanding of the question was. Let Mr. Zimmerman clarify what his question was so Dr. Henck answers what he is asking.

BY MR. ZIMMERMAN:

Q. Dr. Henck, you agree there are solid materials with an intermediate order between that of a liquid and crystal which exhibit diffraction patterns with one low angle peak?

A. I do not agree.

MR. ZIMMERMAN: If we can bring up DX-821.

Q. Dr. Henck, this is an article entitled, "Designing a Molecular Delivery System Within a Preclinical Timeframe."

A. Yes.

Q. Are you familiar with this article?

A. Yes.

Q. You co-authored this article. Right?

A. Yes.
Q. The co-author was Dr. Stephen Bryn, the founder of SSCI, which is the company that did testing for Roche on valganciclovir hydrochloride in 1998 and again for this litigation. Right?
A. 1998? I don't think that's correct.
Q. The SSCI 1998 preformulation report?
A. I thought it was 1996.
Q. The '96 preformulation report Roche did, and the '98 SSCI report?
A. I have to take your word for it. I can't recall.
Q. The document is in evidence. So we won't worry about the date. But it's the same Stephen Byrn?
A. Yes.
Q. This article DX-821, is dated March 2007, and was published in the Journal of Drug Discovery Today. Right?
A. Yes.
Q. And the Journal of Discovery Today is one of the most cited review journals in the field of drug discovery. Right?
A. That's correct.
Q. If we could go to page 190 of your article, you state:

"Liquid crystals and plastic crystals, also referred to mesophases, are solid materials with an order intermediate between that of a liquid and that of a crystal."

Is that right?

A. Yes.

Q. Later on you say:

"Operationally, most pharmaceutical mesophases are birefringent and given an diffraction pattern with one low angle peak and a halo."

That's what you wrote?

A. That's correct.

Q. In all the experiments you did in this case, you were looking for one low angle peak?

A. That's correct.

Q. Were you in the courtroom when Dr. Rogers gave his testimony?

A. Yes.

Q. You agree that Dr. Rogers' testimony that there are solid materials with an intermediate order between that of a crystalline and an amorphous material was accurate and correct; don't you?

A. No, I don't agree. I respectfully do not agree

with Dr. Rogers' statement. What Dr. Rogers described was nucleation and not intermediate order.

Q. If we could turn to page 191 of your article, Dr. Henck, "Designing a Molecular Delivery System Within a Preclinical Timeframe."

On this page, you state:

"Solids can also produce diffuse scattering for amorphous and disordered solids, only diffuse scattering is produced. For systems with intermediate order between crystals and amorphous, a mixture of diffuse scattering and bragg peaks is observed."

And you wrote that; right?

A. Yes.

Q. And by "bragg peaks," you are referring to peaks in an XRD pattern. Correct?

A. Correct.

Q. You have seen Dr. Rogers' plots of the raw data from the Simulated Gastric Fluid Study. Right?

A. Yes.

Q. And you have not taken any issue with the accuracy of Dr. Rogers' plots; have you?

A. No.

Q. Okay. If we look at PTX-766.04, you see the title "Dr. Rogers' assertions," and then it refers to" at least your XRD for the tablet that had been exposed to the simulated gastric fluid for eight minutes being independently scaled?

A. Yes.

Q. You agree that the XRD plot for the eight-minute sample in the gastric fluid study that you prepared was independently scaled; don't you?

A. It was normalized.

Q. It was independently scaled relative to all of the other XRDs from the gastric fluid study. Right?

A. I don't know what your question means because they were normalized.

Q. Did you normalize each XRD for the Simulated Gastric Fluid Study separately and then put it on one plot?

A. Yes.

Q. Or did you normalize them all together?

A. No, they were normalized separately.

Q. Did you normalize each one for the 100 percent value would be the same height?

A. Yes.

Q. Dr. Henck, in all of the simulated gastric fluid studies that you performed, the peak at 3.5 was the

biggest peak in the XRD pattern. Right?
A. For the gastric fluid study?
Q. Yes.
A. Yes.
Q. So if you normalized each one the same, and the biggest peak was always the same height, shouldn't the peak at 3.5 be exactly the same for each XRD in the gastric fluid study if what you are saying is truthful?
A. Yes.
Q. If we could bring up the gastric fluid study PTX-698, the last page.
A. Yes.
Q. I'm sorry. PTX-700, the last page.
A. Yes.
Q. Dr. Henck, are you telling me that the peak at 3.5 in the Simulated Gastric Fluid Study is the same height all the way through?
A. No.
Q. And you just told me a minute ago that if you had normalized them all the same way, the peak at 3.5 would be the same every single time in this experiment. Right?
A. This is correct.
Q. So isn't it true that you independently

normalized each one of these?
A. When you look --
Q. It's a yes or no question.
A. No, it is not a yes or no question because when you look at the X-ray diffraction powder patterns and you look at the X-ray diffractogram, for the four-minute test you will see the peak at 3.5 degrees two theta is not the highest intense peak.
Q. Okay.
A. And that means if you normalize an X-ray diffraction powder pattern, you get the highest peak with 100 percent intensity. In the powder pattern for the four-minute test, for example, when we look at the powder pattern, this is at approximately 20 degrees two theta.
Q. So when you normalized them, you are saying the biggest peak in each one should be the same height?
A. Yes. The biggest peak per X-ray diffraction powder pattern.
Q. Should the biggest peak for the zero time match the biggest peak for the 30-second time match the biggest peak for the one-minute time?
A. Of course not. It can't be. That's why we normalized the X-ray diffraction pattern because what we see during the experiment is the change of the

composition of the tablet.

Q. When you normalize, you take the biggest peak in a pattern and make it 100. Right?

A. Yes.

Q. If we normalize the 30-second time and we normalize the zero time, the biggest peak in the 30-second time should be 100; the biggest peak in the zero time should be 100; and they should be the same height. Right?

A. Yes.

Q. Is that what you are telling me happened here?

A. When we look at the peak at 3.5 degrees two theta for the eight-minute experiment, and we look at the height here and compare it to the height of this peak, when we go from the baseline of the X-ray diffraction powder pattern, I would say, yes, it's approximately the same height.

I'll need to go back and see exactly what it is, but this is what I would expect.

Q. When I asked you on your direct examination the first time, you didn't mention normalization and couldn't remember how you prepared the pattern. When did you learn you normalized the patterns?

A. I look at the raw data first, and like Dr. Rogers did with his analysis, and then I normalized

the X-ray diffraction powder pattern and used this representation for the expert reports that I wrote. So it's about approximately 1 1/2 to two years ago.

Q. But you didn't remember that when you testified previously?

A. No.

Q. And in doing the normalization, how did you choose the height you were going to normalize to?

A. When you normalize an X-ray diffraction powder pattern, you don't choose to normalize the specific peak. You normalize the powder pattern. What normalization does, it puts the highest intense peak at 100 percent and scales the other peak relatively to it.

Q. By normalizing each pattern separately and putting them on the same graph, you change the visual comparison of how the patterns look relative to each other. Correct?

A. No. What I did was, I loaded all these different powder patterns, the raw data, into our software, normalized them, and put them on top of each other to be able to distinguish them. This is what I did.

Q. If we could bring up a side-by-side comparison of PTX-699 and DX-803.8.23.

Dr. Henck, this is Dr. Rogers' data which you admitted you had no issue with, and your data from the spiking study?

A. Right.

Q. If your normalization didn't affect the data, they should show the same thing. Right? They should or shouldn't?

A. They are showing the same thing qualitatively.

Q. And they should show the same relationship between the peak heights. Right?

A. What was that?

Q. Your normalization shouldn't alter the peak height relationship between the graphs. Right?

A. No, this is not correct. Because when you look at the diffraction powder pattern for the tablets, for example, then I choose normalization in this context because what we are comparing are completely different tablets. We are comparing a placebo mixture at the bottom of the X-ray diffraction to three spike samples with 0.1, 0.3, and 0.5 percent crystalline valganci-clovir hydrochloride.

Let me explain, because I think that's important. And then when we look at the X-ray diffraction powder pattern for the two tolerabilities, we see that the normalization is necessary in this

case in order to be able to compare all these different materials with different composition and different history to get a representative picture.

Q. I'm going to make this as easy as I can, and I'm going to try to ask you yes or no questions. If we agree Dr. Rogers' graphs are right?

A. They are correct, yes.

Q. And then yours either maintained the same relationship as Dr. Rogers or they change it. Right?

A. I don't know what you are referring to with regard to relationship.

THE COURT: One at a time, please.

Q. If the .3 spiked standard in Dr. Rogers' test has a smaller peak at 3.5 than the .1 spiked standard, and it is correct, and your data shows a bigger peak at 3.5 for the .3 data than the .1 data, then your scaling, your normalization changed the data from being accurate to something else. Correct?

A. No, this is not correct for a simple reason. These X-ray diffraction powder patterns were measured on the Panalytical instrument in transmission. That means we cannot compare the counts of the X-ray diffraction pattern of one to each other because this would be misleading because the intensity of an X-ray diffraction power pattern depends on the sample

preparation and amount of material used for the sample preparation. So in order to get a representative picture, we need to normalize.

Q. I'm going to ask this very easily: You will agree in Dr. Rogers' plot the .1 crystalline sample has a bigger peak at 3.5 than the .3 sample. Correct?

A. It has a higher intensity.

Q. It has a higher intensity, a larger peak area?

A. This is correct.

Q. And that relationship is straight from the raw data. Correct?

A. That's correct.

Q. And that relationship gets reversed in your plot because of normalization. Correct?

A. That's correct.

Q. So when you normalize, you change the relative peak heights of different samples. Correct?

A. No. This is a representation. I don't change anything.

Q. You represent them differently?

A. Yes.

Q. And when you make the different representation, you then look at them visually to draw conclusions. Correct?

A. Yes.

Q. And, so, whereas the underlying data says you have a bigger, more intense peak at 3.5 for the .1 sample than the .3, your normalization changes the perception of that so that it looks like the .3 has a bigger peak than the .1. Correct?
A. Yes.
Q. And then you drew visual comparisons from that. Correct?
A. Yes.
Q. And you didn't say anything on your graphs they were normalized to change per session?
A. A person skilled in the art would see this because we used an arbitrary Y scale.
Q. When I asked you about the arbitrary Y scale at your deposition and at the trial, you never mentioned normalization. It was only after seeing Dr. Rogers' accurate plots that you remembered you normalized these. Correct?
A. Yes.
Q. And normalization can alter how the relative peak heights are perceived. Right?
A. Yes.
Q. I would like to talk to you a little bit about the issue of magnesium stearate. You talked about the magnesium stearate not being visible in Ranbaxy's

tablets, and you talked about the grade of magnesium stearate.

You will agree whoever made the placebo and the spiked standards for your spiking study at SSCI did not use the same brand and grade of magnesium stearate as is used in Ranbaxy's tablets. Right?

A. Not the exact same manufacturer, that's correct.

Q. You have actually written an article identifying the different types of magnesium stearate. Correct?

A. Yes.

Q. And you have identified them as an anhydrate, a dehydrate, and a dihydrate, a trihydrate?

A. Yes.

Q. In that article you cited, another article by Sharpe, and that article shows that the different forms of magnesium stearate have different peak heights at 3.5 and 5.4. Correct?

A. Yes.

Q. Are you familiar with the article, "Raw Material" by Britton? It's DX-814 in your book.

A. I think I have seen this a long time ago.

Q. If we could look at pages 16 and 17. We'll start with 16.

Does this article discuss that the properties of magnesium stearate can vary based on where it is

from, and, specifically, that material obtained from Italy is amorphous in comparison to those of other countries?

A. Yes.

Q. And on the following page, it shows different XRD patterns for magnesium stearate based on the country of origin?

A. Yes.

Q. And the relative peak heights at 3.5 and 5.4 differ based on country of origin?

A. Yes.

Q. And, so, you'll agree, the lower angle peaks of magnesium stearate vary based on the form of the magnesium stearate and the manufacturer. Correct?

A. That's true.

Q. And you didn't perform any comparison between the magnesium stearate used by SSCI to make the placebo and the spiked crystalline samples in comparison to the magnesium stearate used in Ranbaxy's tablets?

A. That's correct.

Q. And so you have no data to show how the difference in magnesium stearate between those two varies?

A. This is correct.

Q. In PTX-767.06, you state:

"Ranbaxy's tablets will not show a peak at 5.4 degrees in the spiking study because of the nominal concentration of magnesium stearate relative to the amount of valganciclovir hydrochloride."

Right?

A. Can you repeat this?

Q. Here you state that

"Ranbaxy's tablets will not show a peak at 5.4 degrees in the spiking study because of the nominal concentration of magnesium stearate compared to the amount of valganciclovir hydrochloride."

Correct?

A. Yes.

Q. And you cited both DX-551 and DX-552 and you brought those up on the screen in your direct testimony. Right?

A. Yes.

Q. And those are fast scans of Ranbaxy's tablets and placebo over the 2 to 40 degree range. Correct?

A. This is correct.

Q. They are not slow scans over the 3 to 6 degree range as in your spiking study. Right?

A. This is correct.

MR. ZIMMERMAN: If we could bring up DX-553.

Q. Did you consider this data, Dr. Henck, which are Ranbaxy's, in use studies when saying you wouldn't be able to detect peaks for magnesium stearate?

A. No.

Q. Don't Ranbaxy's slow scans from 3 to 6, like your spiking study, always show a peak at 3.5 for magnesium stearate and a peak at 5.4 for magnesium stearate?

A. But these are Ranbaxy's tablets. Right?

Q. The bottom two are Ranbaxy's tablets.

You see the peak at 3.5 and the peak at 5.4?

A. And the two at the top are the ones with 0.5 percent crystalline valganciclovir hydrochloride.

Q. Spiked in placebo?

A. So how can you distinguish between valganci-clovir hydrochloride and magnesium stearate?

Q. In the bottom two we are looking at Ranbaxy's tablets?

A. Yes.

Q. Are you saying the peak at 5.4 in Ranbaxy's tablets could be from something other than magnesium

stearate?
A. No, that's not what I'm saying. I'm referring to the peak at 3.5 and 3.6 degrees two theta.
Q. Let's back up.
We agree in Ranbaxy's slow scans you see a peak at 5.4 for magnesium stearate?
A. That's correct.
Q. Now, if we look at your plot from the spiking study, PTX-699, last page, the top two are Ranbaxy's tablets. Correct?
A. This is correct.
Q. And we see a peak at 5.4?
A. This is correct.
Q. And that's for magnesium stearate?
A. This can be for magnesium stearate, yes.
MR. ZIMMERMAN: If we can bring up 767.06 again, PTX, Ranbaxy's tablets.
Q. (Reading.)
"Ranbaxy's tablets will not show peaks for magnesium stearate at 3.6 or 5.4 degrees two theta."
A. Yes.
Q. When you say that, you are dead wrong because your own spiking study shows a peak at 5.4 in Ranbaxy's tablets. Right?

MR. ZIMMERMAN: And if we could bring up PTX-699.

Q. That's your spiking study data, and the top two are Ranbaxy's tablets, and they show a peak at 5.4 for magnesium stearate; don't they?

A. We don't have a peak in the placebo that contains magnesium stearate.

Q. In your demonstrative, you didn't say placebo. My question was: In the top two Ranbaxy's tablets, you see a peak at 5.4 degrees two theta for magnesium stearate?

A. I see a peak at 5.4 degrees two theta, and it could be due to magnesium stearate.

Q. Is there anything else in Ranbaxy's tablets that you know of that could cause that peak?

A. I don't know.

Q. As an expert for Roche in this case, you have looked at all the components of Ranbaxy's tablets. Is there anything else in the tablets that had a peak at 5.4 that could cause what we are seeing in Ranbaxy's tablets in your spiking study?

A. No.

Q. If you look at the spike samples -- the .1, the .3, and .5, we see a peak at 5.4 approximately again. Correct?

A. It varies. It is not -- here for the 3.6 degrees compared to 5.4 degrees two theta.
Q. It is in the region of 5 and 5.6. Right?
A. Yes.
Q. Is there anything else in those spike standards that could cause that peak other than magnesium stearate?
A. No.
Q. Okay. So we see a peak in Ranbaxy's tablets in your spiking study for magnesium stearate. We see a peak in all of the spiked samples from the magnesium stearate. When we look at the placebo, why don't we see a peak at 5.4 from the magnesium stearate?
A. I don't know.
Q. In the placebo, the concentration of magnesium stearate is higher than any of the other components in the spiking study. Correct?
A. Yes.
Q. So if we saw a peak at 5.4 for magnesium stearate, it should be the biggest in the placebo. Right?
A. It should be.
Q. And that's not what we see?
A. Exactly.
Q. And you have absolutely no idea why the placebo

doesn't show that peak at 5.4?
A. I don't know.
Q. Isn't it because something is wrong with the placebo?
A. It doesn't have to. The peak at 3.6 degrees two theta is in the original magnesium stearate is a very weak peak. So depending on sample preparation, depending on the conditions that were chosen, it is not necessary that we see the same peak ratio between these two peaks in every sample. So why we don't see the peak at 3.6 and 5.4 degrees two theta in this experiment, I don't have an explanation for it.
Q. And you agree that the placebo should show a peak at 5.4 from the magnesium stearate?
A. I don't know whether I should agree. The data does not show a peak for the placebo.
Q. Given that all the other samples do, and the concentration of magnesium stearate in the placebo is bigger than all the other samples, we should see a peak in the placebo at 5.4 for magnesium stearate; shouldn't we?
A. It would not surprise me if we would see one.
Q. I'm asking you if we should see it.
A. We should see a peak.
Q. And the placebo in your spiking study, the XRD,

was run nearly 3 1/2 months after the placebo was actually prepared. Correct?

A. Yes.

Q. And the placebo is the baseline for all the comparisons in your spiking study. Right?

A. It's not a baseline. It's a comparison to the other materials in this study. This is not a quantitative assessment. It's a qualitative assessment.

Q. After you got the data for the spiking study, didn't you ask somebody to go back and run the placebo so you would have something to compare everything else to? Right?

A. Yes.

Q. So the placebo is the baseline you used for comparison. Right?

A. I wouldn't call this a baseline. You call this a baseline. I'll not call this a baseline.

Q. I'd like to talk to you for a minute on the single peak issue.

In all of the articles you referred to, none of them were identifying whether crystalline material was present in an unknown sample using one peak. Correct? They were all analyzing known mixtures?

A. That's correct.

Q. In we could look at your gastric fluid study for just a minute, PTX-766.02.
A. Yes.
Q. You don't disagree with Dr. Rogers with respect to what the processing times were as reflected by the LIMS report. Right?
A. Can you repeat your question?
Q. You don't disagree that the 30-second gastric fluid sample took 22 minutes to process, as reflected in the LIMS report. The other ones took 10, 11, and 12 for the one-, two-, and four-minute samples respectively?
A. Yes.
Q. That data comes right out of the LIMS reports that you prepared at SSCI?
A. This is correct.
Q. As a GMP facility, you would have to have those time-stamped. Right?
A. Yes.
Q. Can you tell me why those time stamps don't exist for the eight- and the 15-minute?
A. No, I don't know why they do not exist. I'm pretty sure they can be found. I'm not quite sure why they were not -- they were not available in this context.

Q. If we could bring up PTX-700, last page.
A. Yes.
Q. Dr. Henck, you agree that for the 30-second sample, the light blue one, the peak at 3.5 is much bigger than the one-minute, two-minute, four-minute peak at 3.5. Right?
A. That's correct.
Q. It's about twice as big; isn't it?
A. Yeah, roughly.
Q. And the 30-second sample, it took 22 minutes to process from the time it was pulled out of the gastric fluid to the time XRD was done. And you would agree for the one-minute, two-minute, and four-minute samples, the peak at 3.5 is about the same height. Right?
A. Yes.
Q. And those took 10, 11, and 12 minutes to process. So about the same time. Correct?
A. Yes.
Q. Doesn't that data, isn't that consistent with the peak at 3.5 not being caused by being in the gastric fluid, but the length of time it takes from the time you pull it out to finish the processing?
And I'm not asking if it is or isn't. I'm asking if the data is consistent with that.

A. If the data is consistent with your assessment?
Q. Yes.
A. It is consistent with your assessment, but I would use a different explanation for it.
Q. And what we see is, from your data, is that the peak height at 3.5 gets bigger the longer it takes to process the sample after removal from the gastric fluid. Correct? That's what the data shows. Correct? It's a yes or no question.
A. Up to four minutes -- your question would include up to four minutes, but would exclude eight and 15 minutes?
Q. Yes, because we have no idea what the processing times were, because in violation of GMP, SSCI didn't keep that data.
A. I don't think it's a violation of GMP.
Q. We don't have processing times for the eight and 15 minutes.
A. I don't know.
Q. What we do see is the longer it takes to process after you pull it out of the gastric fluid, the bigger the peak at 3.5. Right?
A. Yes.
Q. I would like to address two other points very quickly, Dr. Henck.

PTX-763, the limit of detection from the FDA guidance you presented. If we could go to page 7 of that document.

If we could go under Step A and highlight, quote, based on visual evaluation, quote, the last sentence which you didn't read, Dr. Henck, is:

> "The detection limit is determined by the analysis of samples with known concentrations of analyte, and by establishing the minimum level at which the analyte can be reliably detected."

What is the minimum level in the spiking study at which crystalline valganciclovir hydrochloride can be reliably detected?

A. According to my study, somewhere between 0.1 and 0.3.

Q. Do you have documentation where you established that and that it was reliable?

A. This was just by the visual inspection.

Q. Doesn't the guidance that you refer to say if you are going to use visual inspection, you have to establish that the minimum level of analyte can be reliably detected? Did you do multiple studies to do that?

A. We did 0.1, 0.3, and 0.5 percent spiking study.
Q. So you ran the spiking study once, and it's your position that satisfied the FDA guidelines?
A. Yes.
Q. I do have one last question: On any of the samples that were ground --
A. Rendered into a powder.
Q. I say "ground"; you say "rendered" into a powder. We'll agree to disagree on that one.
On any of the samples where the opadry coating was ground in, did you actually see the sample?
A. Yes.
Q. And when the opened opadry came off, it was like a plastic shell?
A. It was flaky.
Q. It's like a plastic and comes off all at once?
A. No.
Q. When you hit it on the top, it doesn't peel away?
A. No, not every time. No.
Q. Not every time; most times?
A. Sometimes.
Q. Doesn't it take a lot of force to grind up the plastic opadry coating?
A. Obviously, you never have done this. No, it

doesn't take a lot of force.
Q. You are sure, based on what you saw?
A. Yes.
Q. And do you end up with a white powder with orange flakes in it or a homogenously orange powder?
A. You end up with a white powder that has orange cores in it.
Q. Orange flakes?
A. Orange cores.
Q. And they differ in size, the orange pieces, relative to the white ones?
A. Yes.
Q. So it is not a homogenous mixture that's being tested when you grind the opadry in it?
A. It is. The coating has a different particle size; but because of the sample preparation, you analyze most of the sample, which means in this context because of spinning of the samples, we make sure we get a homogenous representation of the sample.
Q. But the powder doesn't have a uniformed particle size?
A. That's correct.
Q. And it's not homogenous, is it?
A. That's correct.
MR. ZIMMERMAN: I have no further questions.

REDIRECT EXAMINATION

BY MR. PEZZANO:

Q. Dr. Henck, do you recall your testimony that normalization can change how relative peak heights are perceived in connection with the crystalline seed study?

A. Yes.

Q. And does normalization have any effect on the ability of a person skilled in the art to tell qualitatively whether a peak at a given two theta angle is present?

A. No, absolutely not.

Q. Does normalization have any effect on a person skill in the art's ability to tell qualitatively whether valganciclovir hydrochloride is present?

A. No.

Q. I want to direct your attention to PTX-700. These are your results on the Simulated Gastric Fluid Study?

A. Yes.

Q. Let's go to the last page.

You offered to give an explanation concerning the following:

What explanation would you give as to why the height of the peak in the 30 second peak that was in

your LIMS reports as being analyzed in a 22-minute timeframe, why the height of that peak is higher than the other peaks at one-minute, two minutes, four minutes, whereas the timeframe in the LIMS report is documented at 10 to 12 minutes before the tablet is taken out of the simulated gastric fluid and tested by XRD?

A. First of all, this is a qualitative analysis, and we cannot perform all the experiments on one tablet. So these are individual tablets that I exposed at different times to the simulated gastric fluid, and these tablets behave differently individually.

We know this because they are taking up water over time in a different way, and so for the first sample we have a different composition than we have for the other samples, and all these kinds of effects will contribute to changes in the peak height at 3.5 degrees two theta.

Q. And the effect on the changes in the peak height is caused by the simulated gastric fluid and being in the simulated gastric fluid or the ambient conditions outside of the simulated gastric fluid?

A. They are caused by the gastric fluid and because the ambient conditions, as we have shown many times,

do not impact on this short time scale the appearance of crystalline valganciclovir hydrochloride.

MR. PEZZANO: I have no further questions.

MR. ZIMMERMAN: I have no questions, your Honor.

I would move to admit DX-821.

THE COURT: And Mr. Pezzano has some exhibits to put in.

Any objection to the exhibit Mr. Zimmerman just referred to?

MR. PEZZANO: I have no objection.

THE COURT: All right. That's in evidence.

(Defendants' Exhibit No. DX-821 was received in evidence.)

MR. PEZZANO: The exhibits I'm offering into evidence are: PTX-752, 763, 764, 765, 766, 767 -- and I'll note for the record 764 through 767 are demonstratives, for illustrative purposes only -- PTX-768, PTX-716, PTX-770, PTX-772 and DX-603.

MR. ZIMMERMAN: No objection, your Honor.

THE COURT: All right. They will be admitted except for the demonstratives.

(Plaintiff's Exhibits Nos. PTX-752, PTX-763, PTX-768, PTX-716, PTX-770, PTX-772 and DX-603 were received in

evidence.)

THE COURT: You are excused Dr. Henck. You may step down.

(Witness excused.)

THE COURT: That concludes the testimony.

MR. PEZZANO: It does.

Also, the parties over the weekend discussed a proposal on the briefing schedule.

MR. ZIMMERMAN: And we would be happy to send it to you in a letter.

THE COURT: I can do a conference call on January 5th when I return. My suggestion is you not agree on a schedule and actually take the holidays off, which is why I wasn't going to discuss it with you today.

MR. PEZZANO: There is one point; the briefing is all contingent upon Ranbaxy represented to your Honor they would not be coming on the market until the earliest January 15, and Ranbaxy's counsel represented to us this weekend -- I'll leave the representation up to them because that impacts on the briefing schedule, and I believe it is appropriate we get a representation now so we can work on this briefing schedule.

MR. ZIMMERMAN: Your Honor, we have a proposed briefing schedule. The January 15 time gives us

plenty of time. Ranbaxy will agree not to come on the market prior to April 1st to give us enough time to do a briefing schedule.

THE COURT: Remember, whatever your briefing schedule is, you have to build in my schedule.

MR. ZIMMERMAN: Yes, and that's all I have authorization for today.

THE COURT: Okay.

MR. ZIMMERMAN: The other one is, we do have deposition designations from Ranbaxy that we held for our case, if I could submit those.

THE COURT: Bring those up.

Did I ever get the briefing on the nonobviousness? I never got handed it. Is this it over here in the corner?

MR. ZIMMERMAN: We E-file it, your Honor.

THE COURT: Okay.

MR. DOUGHERTY: Roche has a couple of things to hand up also.

We have a CD with the list of all of the Roche exhibits that had been admitted prior to today, so we can hand that up. That will be, of course, updated.

THE COURT: Wait. Send me one CD, and I did say I would take the exhibits by CD. You could each do this now and get it ready. I'm away until the 5th.

MR. DOUGHERTY: In addition to that, we would like to hand up a CD of the joint deposition designations along with a CD of the video clips of Ranbaxy's witnesses that Roche played at trial.

THE COURT: That's fine.

You can submit to me the exhibits on CDs, both of you, in January. That's fine.

Let's plan on either Monday, the 5th, or Tuesday, the 6th, that we will have a call. She will get in touch with you and work that out. We have to deal with timing, right, California people, so it will be late morning or early afternoon.

Okay. Thank you for all your cooperation during the trial. I think it went pretty smoothly, and you finished on time. I appreciate it.

If I need to enter an order, I think you people should take the holidays off. No briefing until January.

Thank you very much. Have a good holiday.

THE CLERK: All rise.

(Proceedings concluded at 4 p.m..)

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I N D E X

E X H I B I T S

C E R T I F I C A T E

I, **Vincent Russoniello**, Official United States Court Reporter and Certified Court Reporter of the State of New Jersey, do hereby certify that the foregoing is a true and accurate transcript of the proceedings as taken stenographically by and before me at the time, place and on the date hereinbefore set forth.

I do further certify that I am neither a relative nor employee nor attorney nor counsel of any of the parties to this action, and that I am neither a relative nor employee of such attorney or counsel and that I am not financially interested in this action.

S/Vincent Russoniello
Vincent Russoniello, CCR-R
Certificate No. 675
Date: April 22, 2009